201-15898B

I U C L I D

Data Set

Existing Chemical	:	ID: 79-46-9
CAS No.	:	79-46-9
Producer related part		
Company	:	The Dow Chemical Company
Creation date	:	11.04.2005
Substance related part		
Company	:	The Dow Chemical Company
Creation date	:	11.04.2005
Status	:	
Memo	:	2-Nitropropane
Printing date	:	11.05.2005
Revision date	:	
Date of last update	:	11.05.2005
Number of pages	:	80
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	manufacturer
Name	:	Dow Chemical Co.
Contact person	:	Dr. William T. Stott
Date	:	11.05.2005
Street	:	1803 Building
Town	:	48674
Country	:	United States
Phone	:	989 636 1000
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

Reliability : (1) valid without restriction
11.05.2005

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	Propane, 2-nitro
Smiles Code	:	O=N(=O)C(C)C
Molecular formula	:	C3-H7-N-O2
Molecular weight	:	89.09
Petrol class	:	

Source : PCA Services, Inc Durham, NC
06.12.2003

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	
Substance type	:	inorganic
Physical status	:	liquid
Purity	:	ca. 96 % w/w
Colour	:	Colorless
Odour	:	Pleasant fruity odor

Source : PCA Services, Inc Durham, NC
11.04.2005 (1)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

2-Nitropropane

Source : PCA Services, Inc Durham, NC
06.12.2003

dimethylnitromethane

Source : PCA Services, Inc Durham, NC
06.02.2004

isonitropropane

Source : PCA Services, Inc Durham, NC
06.02.2004

nitroisopropane

Source : PCA Services, Inc Durham, NC
06.02.2004

1.3 IMPURITIES

1.4 ADDITIVES

Remark : No additives known
Source : PCA Services, Inc Durham, NC
Reliability : (2) valid with restrictions
06.12.2003

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : industrial
Category : other: C4 Taggant Manufacturing

Remark : Less than 1% of the total 2-nitropropane is sold for use in C4 taggant manufacturing processes and in research facilities.
Reliability : (2) valid with restrictions
11.04.2005

Type of use : industrial
Category : other: chemical intermediate

Remark : More than 99% of 2-nitropropane is used as a chemical intermediate in Dow's own manufacturing processes.
Reliability : (2) valid with restrictions
11.04.2005

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

Origin of substance : Synthesis
Type : Production

Remark : The manufacturing operation is a continuous process. During production, propane and nitric acid are reacted at high temperature and high pressure (370oC and 150 psig). This reaction results in a mixed stream of nitroparaffins of which 2-NP represents 55-62%. The 2-NP is removed from the other nitroparaffins through distillation. Following the separation, the 2-NP is piped directly to storage tanks. From these tanks the majority is then piped to other plants for use as a chemical intermediate.
Source : The Dow Chemical Company, Midland, MI. 2005.
Reliability : (2) valid with restrictions
11.04.2005

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	= -91.3 °C
Sublimation	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(2) valid with restrictions Data were obtained from a standard literature reference on physical properties.
Flag	:	Critical study for SIDS endpoint

11.04.2005 (2) (3)

Value	:	= -93 °C
Sublimation	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(2) valid with restrictions Data were obtained from a standard literature reference on physical properties.

11.04.2005 (4)

2.2 BOILING POINT

Value	:	= 120.3 °C at 1013 hPa
Decomposition	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(2) valid with restrictions Data were obtained from a standard literature reference on physical properties.
Flag	:	Critical study for SIDS endpoint

11.04.2005 (2) (3)

Value	:	= 120.3 °C at 1013 hPa
Decomposition	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(2) valid with restrictions Data were obtained from a standard literature reference on physical properties.

06.12.2003 (4)

2.3 DENSITY

Type : relative density
Value : = .988 g/cm³ at 25 °C
Method :
Year : 1955
GLP :
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Data from a handbook or collection.
11.04.2005 (3)

Type : relative density
Value : = .9821 g/cm³ at 25 °C
Method : other
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : PCA Services, Inc Durham, NC
Reliability : (2) valid with restrictions
Data from a collection.
11.04.2005 (5)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = 17.32 hPa at 20 °C
Decomposition :
Method :
Year : 1949
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Data from a collection
11.04.2005 (6)

Value : = 23.03 hPa at 25 °C
Decomposition :
Method :
Year : 1949
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Data from a collection
11.04.2005 (6)

Value : = 26.7 hPa at 25 °C
Decomposition :
Method :
Year : 1981

GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(2) valid with restrictions Data were obtained from a standard literature reference on physical properties.

11.04.2005 (7)

Value	:	= 10 hPa at 10.7 °C
Decomposition	:	
Method	:	other (calculated)
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Vapor pressures at various temperatures are: -48 Degrees C: 10 Pa* -22 Degrees C: 100 Pa* 55.6 Degrees C: 100 hPa 119.8 Degrees C: 1000 hPa * Indicates an extrapolation beyond the region where experimental measurement exist.
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(2) valid with restrictions Data were obtained from a standard literature reference on physical properties.

11.04.2005 (2)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= 1.35 at °C
pH value	:	
Method	:	OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year	:	1996
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The partition coefficient is defined as the ration of the equilibrium concentration of a dissolved substance in a two-phase system consisting of two largely immiscible solvents. For the determination of the Pow about 50 mg was weighed in a flask. After addition of water and n-octanol, the two-phase system was agitated for 30 minutes. After one hour, phase separation at 20C the concentration in the octanol phase and in the water phase have been determined by gas chromatography. The Pow was calculated based on the average of two trials.
Reliability	:	(2) valid with restrictions 2 guideline study with acceptable restrictions (not GLP)
Flag	:	Critical study for SIDS endpoint

18.04.2005 (8) (9)

Partition coefficient	:	octanol-water
Log pow	:	= .87 at 20 °C

pH value	:	= 7
Method	:	other (calculated)
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Inputs to the program are CAS No. 79-46-9 and measured values for melting point (-91.3 degrees C), boiling point (120.2 degrees C), vapor pressure (20 mm Hg), and water solubility (17,400 mg/l).
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(2) valid with restrictions Data were obtained from a standard literature reference on physical properties.

06.12.2003 (10)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 17400 mg/l at 25 °C
pH value	:	= 7
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(2) valid with restrictions Data were obtained from a standard literature reference on physical properties.
Flag	:	Critical study for SIDS endpoint

11.04.2005 (2)

Solubility in	:	Water
Value	:	= 17000 mg/l at °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(2) valid with restrictions Data were obtained from a standard literature reference on physical properties.

11.04.2005 (11)

Solubility in	:	Water
Value	:	= 1.7 other: wt% at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	
Year	:	1955
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Data from a collection.

11.04.2005 (3)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	Sun light
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	= .00000000000017 cm^3/(molecule*sec)
Degradation	:	= 50 % after 63.6 day(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Inputs to the program are CAS No. 79-46-9 and measured values for melting point (-91.3 degrees C), boiling point (120.2 degrees C), vapor pressure (20 mm Hg), and water solubility (17,400 mg/l).
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(2) valid with restrictions Data were obtained from a standard estimation program.
Flag	:	Critical study for SIDS endpoint

06.12.2003 (12)

Type	:	
Light source	:	other: mercury vapor lamp
Light spectrum	:	> 290 nm
Relative intensity	:	based on intensity of sunlight
DIRECT PHOTOLYSIS		
Halflife t1/2	:	
Degradation	:	= 32.2 % after 17 hour(s)
Quantum yield	:	
Deg. product	:	
Method	:	
Year	:	1988
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The 14-C-radiolabelled chemical was adsorbed homogenously on silica gel by rotating the mixture in a flask for a few hours. The mixture was irradiated in a photoreactor for 17 hours with the light of a mercury vaporlamp, filtered through Pyrex glass (lamda > 290 nm). The evolved CO2 and volatile organic fragments were collected in corresponding adsorbents. The radioactivity of the collected materials and of the silica gel was determined and calculated as percentage of the radioactivity of the starting material.
Reliability	:	(2) valid with restrictions

27.04.2005 (13)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	at °C

t1/2 pH9 : at °C

Remark : Inputs to the program are CAS No. 79-46-9 and measured values for melting point (-91.3 degrees C), boiling point (120.2 degrees C), vapor pressure (20 mm Hg), and water solubility (17,400 mg/l).

Result : 2-Nitropropane does not have any functional groups that have been found to hydrolyse or degrade in water at room temperature and neutral pHs. The organo-nitro group is stable to water under these conditions.

Source : PCA Services, Inc Durham, NC
06.12.2003 (14)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media :
Air : 70.5 % (Fugacity Model Level I)
Water : 29 % (Fugacity Model Level I)
Soil : .6 % (Fugacity Model Level I)
Biota : .1 % (Fugacity Model Level II/III)
Soil : 3.2 % (Fugacity Model Level II/III)
Method : other
Year : 2003

Method : METHOD
Test: Prediction of Equilibrium Environmental Distribution
Method: Level I Fugacity Model
Year: 1999
Remarks: Level I model version 2.11, Obtained from the Canadian Environmental Modeling Centre, Trent University, Peterborough, Ontario, Canada.

Input Parameters for Level I Model:

Property	Value	Source
Data Temperature (°C)	25	Default environmental temperature
Chemical Type	1	indicates chemical can partition into all environmental compartments
Molecular Mass (g/mol)	89.09	Calculated from molecular structure
Water Solubility (g/m3)	17,000	Measured value reported in [1]
Vapor Pressure @ 25°C	2,300 Pa	Measured value reported in [1]
Melting Point (C)	-91.3	Measured value reported in [1]
Henry's Law Constant	12.1(Pa*m3/mole)	Calculated by Level I model [2]
Log Kow	1.35	Measured value reported in [3]
Simulated Emission (kg)	100,000	Level I default value [2]
Simulated Environment	Default Level I environment [2]	

In addition to the model inputs above, the following Reaction Half-lives (hr)

were used for the Level III Model:
Air (vapor phase) 987 [1]
Water (no susp. solids) 3,600*
Soil 7,200*
Sediment 7,200*
Suspended Sediment **1.0 x 10^11
Fish **1.0 x 10^11
Aerosol **1.0 x 10^11

[1] Estimated half-life for indirect photolysis.
*Estimated half-lives in water, soil, and sediment extrapolated from predicted inherent biodegradability reported.
*Half-lives extrapolated from predicted inherent biodegradability, according to Technical Guidance Document of the European Commission [4].
**Default value used in Level III model when reaction is expected to be negligible in this compartment

Result : Level I: Predicted equilibrium distribution among air, water, soil, and sediments

Emission Scenario: 100,000 kg total emissions
Percentage and amount distributed to

Air	Water	Soil	Sediment
70.5%	29.0%	0.6%	<0.1%
7.0 x 10^4 kg	2.9 x 10^4 kg	5.7 x 10^2 kg	13 kg

This substance has high water solubility, moderate vapor pressure, and low log Kow. In the absence of advective and reactive processes, these physical properties dictate that the substance will be distributed primarily among the air and water compartments at equilibrium. The substance has a low potential for adsorption to soil or sediments, and moderate potential to volatilize from water.

Level III: Predicted distribution among air, water, soil, and sediments

Emission Scenario
Percentage and amount distributed

1,000 kg/hr to Air (most likely scenario)
Air 91.8%
2.0 x 10^3 kg
Water 5.0%
1.1 x 10^2 kg
Soil 3.2%
70 kg
Sediment <0.1%
<1 kg
Residence Time (days) 0.1 (without advection=98)

1,000 kg/hr to Water
Air 0.2%
8.1 x 10^2 kg
Water 99.8%
5.0 x 10^5 kg
Soil <0.1%
29 kg
Sediment <0.1%
2.4 x 10^2 kg
Residence Time (days) 21 (without advection=216)

1,000 kg/hr to Soil
Air 0.3%
1.6 x 10^3 kg
Water 32.2%
1.5 x 10^5 kg
Soil 67.5%
3.2 x 10^5 kg
Sediment <0.1%
76 kg
Residence Time (days) 20 (without advection=325)

1,000 kg/hr simultaneously to Air, Water, and Soil
Air 0.4%
4.4 x 10^3 kg
Water 66.6%
6.5 x 10^5 kg
Soil 32.9%
3.2 x 10^5 kg
Sediment <0.1%
3.2 x 10^2 kg
Residence Time (days) 14 (without advection=257)

CONCLUSIONS
Remarks: This substance has high water solubility, moderate vapor pressure, and low log Kow. The substance therefore has a low potential for adsorption to soil or sediments, and moderate potential to volatilize from water or soil to the atmosphere. If released to air (the most probable emission route), 2-nitropropane will remain primarily in the atmospheric compartment, with some deposition to surface water and soil. 2-Nitropropane is slowly reacted in the atmosphere, and therefore advection is the dominant process affecting atmospheric fate. If released directly to water, the substance will remain dissolved in water and is expected to be ultimately biodegraded. If released to soil, 2-nitropropane will be primarily dissolved in soil pore water (groundwater), and is expected to be ultimately biodegraded.

Source : PCA Services, Inc Durham, NC
Reliability : (2) valid with restrictions
Fugacity data were obtained using a standard Fugacity Level III model program with appropriate inputs.
Flag : Critical study for SIDS endpoint
11.05.2005 (15)

Type :
Media :
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other
Year :

Result : Henry's Law constant (1.19X10-4 atm-cu m/mole)
Source : PCA Services, Inc Durham, NC
Reliability : (2) valid with restrictions
06.12.2003 (16)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge, domestic, non-adapted
Concentration	:	2 mg/l related to Test substance related to
Contact time	:	28 day(s)
Degradation	:	< .1 (±) % after 28 day(s)
Result	:	under test conditions no biodegradation observed
Kinetic of testsubst.	:	5 day(s) = .1 % 15 day(s) = .1 % 28 day(s) = .1 % % %
Control substance	:	other: LAS (not defined)
Kinetic	:	5 day(s) = 61.8 % 28 day(s) = 68.3 %
Deg. product	:	
Method	:	OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year	:	1990
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The test was valid since the positive control (LAS) was degraded by > 60%. 2- nitropropane was degraded by < 0.1% at 5, 15 and 28 days. Therefore, the material was not readily biodegraded.
Source	:	PCA Services, Inc Durham, NC
Test condition	:	Test material was dissolved at a concentration of 2 mg/l in a nutrient solution, which was prepared from aerated deionized water (9 ml O2/l), nutritive salts (not specified) and trace element (not specified) solutions. The solution was inoculated with one drop of inoculum from the effluent of a municipal sewage water treatment plant. Control systems containing nutrient solution only, nutrient solution and inoculum and nutrient solution, inoculum and a positive control material (LAS) also were prepared. The identity of LAS and the concentration tested were not listed. Each condition was tested in duplicate. The test containers were stored in the dark at 20 - 21 degrees C and the concentration of oxygen was measured with an oxygen electrode at day 0 (start), day 5, day 15 and day 28 (end of test). At each time, the oxygen demand of the test material was determined for each test condition. The amount of biodegradation (in percent) was calculated from the results of each determination and the theoretical oxygen demand. According to the guideline, deionized water should have been used in the experiment. However, the carbon content of the water (up to 40 ppb) varied too much to be used. Therefore, distilled tap water was used in the experiments. No further details were mentioned.
Reliability	:	(2) valid with restrictions The purity of the test material, the TOD and the method of determining the TOD were not mentioned.
Flag	:	Critical study for SIDS endpoint

06.01.2004 (17)

Type	:	aerobic
Inoculum	:	other:sludge
Concentration	:	2 mg/l related to Test substance 9.9 mg/l related to Test substance
Contact time	:	28 day(s)
Degradation	:	= 8 - 14 (±) % after 28 day(s)
Result	:	other: not readily boidegradable
Deg. product	:	
Method	:	other: CITI Closed Bottle Test
Year	:	1992
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	A closed bottle test was conducted with 2.0 or 9.9 mg/l test material and 2 mg As/l sludge. The amount of biodegradation was determined by BOD after 28 days. the results for 2.0 and 9.9 mg/l were 14% and 8%, respectively.
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(2) valid with restrictions Test conditions are not described in detail. Purity of the material is unknown.

06.02.2004 (18)

Type	:	aerobic
Inoculum	:	activated sludge, domestic, non-adapted
Concentration	:	50 µg/l related to Test substance related to
Contact time	:	5 day(s)
Degradation	:	= .8 (±) % after 5 day(s)
Result	:	under test conditions no biodegradation observed
Deg. product	:	
Method	:	other: degradation in activated sludge (GSF test)
Year	:	1986
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The test was performed according to a method developed by the GSF Institute for Ecological Chemistry in Munich, West Germany. Although a positive control was not tested in the study, other nitroalkanes that were tested were biodegraded to some exxtent (although they were not readily biodegraded). The recovery rate of radioactivity in the experiment was considerably lower than that of other nitroalkanes tested in the same experiment (range of 73.1 - 83.8%).
Result	:	The amount of material degraded to CO2 was 0.4%, 0.6% and 1.5%, for an average of 0.8%. The average concentrations of material in the water, sludge and adsorbent were 15.6%, 0.7% and 30% of the starting material, respectively. Therefore, the average recovery rate was 47.0%. The recovery rate in the adsorbent was significantly lower than that for other nitroalkanes tested in the same experiment.
Source	:	PCA Services, Inc Durham, NC
Test condition	:	14C-radiolabeled test material was synthesized by the GSF Institute for Ecological Chemistry. The activity was not mentioned. The radiolabeled test material was added to a suspension of activated sludge (1 g dry weight/liter) at a concentration of 50 ppb. The activated sludge suspension was cultivated with a nutrient solution to which fresh activated sludge from a municipal sewage treatment plant was added weekly. The test mixture was stirred for 5 days in a closed container maintained at 25 degrees C.

The evolved CO2 was absorbed on soda lime. Upon termination, the radioactivity in 10 ml samples of the aqueous samples, combined with 10 ml of scintillation fluid were measured by a scintillation counter. Solid samples were combusted to 14C-CO2, wich was absorbed in a commercial absorbent (phenylethylamine basis) and the radioactivity was counted directly. The degradation to CO2 (in percent) was calculated as the ratio between the radioactivity of the CO2 evolving from the adsorbent upon acidification and the radioactivity of the starting material. The test was performed in triplicate. No other details were provided.

Test substance : Test material was used as supplied by Merck (Darmstadt, West Germany). It is assumed that the material was of high purity due to the source.

Reliability : (4) not assignable
Test details are lacking. A positive control wasn't tested. The results could have been affected by the low recovery rate of the radioactivity.

06.01.2004 (19)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species : Leuciscus idus melanotus (Fish, fresh water)
Exposure period : 3 day(s) at °C
Concentration :
BCF : = 1
Elimination :
Method :
Year : 1988
GLP :
Test substance : as prescribed by 1.1 - 1.4

Method : Five fish were placed in a closed system containing 50 ppb solution of the test material in 8L water which was stirred gently to improve air exchange between the aqueous layer and the headspace. The fish were fasted during the three day exposure. Upon termination of the experiment, the radioactivity in the fish and in the water was determined, and the accumulation factor BF3 was calculated in analogy to the test degradation and accumulation in activa ted sludge.

Reliability : (2) valid with restrictions
27.04.2005 (13)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	> 612.5 measured/nominal
Limit test	:	no
Analytical monitoring	:	yes
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The reference was a review article that contained results of studies performed with 40 chemicals over a two year period.
Result	:	The only result given was the fact that there was "no significant mortality" below 612.5 mg/l. This is interpreted to mean that the LC50 value was > 612.5 mg/l. It is assumed that this was the highest concentration tested. The concentrations of material measured at the beginning and end of the test and the pH values and dissolved oxygen concentrations over the course of the study were not listed.
Source	:	PCA Services, Inc Durham, NC
Test condition	:	Fish: The fathead minnows were raised from controlled breeding stocks at the EPA Newtown Fish Toxicology Station, Cincinnati, OH. They were observed for a minimum of 14 days before use. They were acclimated to test water over 4 days by withdrawing water from the acclimation tanks and replacing it with test water twice daily. Temperatures were gradually lowered to 22 +/- 1 degrees C. Over the last 2 days of acclimation, the water was 100% test water at 22 degrees C. If more than 3% mortality occurred during this period, the organisms were not used for testing. Water: Reconstituted water of 40 -48 mg/l hardness (as CaCO3), 30 -35 mg/l alkalinity (as CaCO3), 120 -160 microSiemens/cm conductivity and pH 7.2 - 7.9 was used. Test conduct: Vessels were filled with 12 liters of dilution water to a depth of 24 cm. The containers were then placed in a large circulating temperature bath for cooling to 22 +/- 1 degrees C. Test material (at least 5 concentrations in a 0.6 geometric series) was added when the temperature had equilibrated. Actual concentrations tested were not listed. The solutions were briefly stirred with a glass rod, and a sample was removed for determination of concentration of test material by ultraviolet absorbance at 278 nm. Five fish were then placed in each of two duplicate aquaria, for a total of 10 tested per concentration. At least 2 control aquaria containing a total of 10 organisms were prepared. During the 96 hour test period, deaths were to be recorded and the bodies removed when noticed. At each 24 hour period, the number of surviving fish, dissolved oxygen and temperature were measured or noted. At the end of the test period, pH was measured and a water sample was analyzed for concentration of test material. The control organisms were then weighed and measured to determine their average size. The 96 hour LC50 values and confidence limits were to be calculated using either the probit, moving average or binomial test method (depending on the number of deaths observed).

Analysis of test concentrations: Initially, water samples were not filtered before analysis so that the total concentration of test material in the water column could be determined. It was later decided that all water samples should be filtered through 0.45 micron filters before analysis. It is not known if the samples were unfiltered or filtered before analysis of nitromethane. The relative error and standard deviation for the analysis were 6.8 (it is assumed that this is %) and +/- 3.2, respectively.

Reliability : (2) valid with restrictions
The purity of the test material was not listed. The system was not closed. It is unknown how much material was lost to volatization over the course of the study.

Flag : Critical study for SIDS endpoint

07.01.2004 (20)

Type : static
Species : Brachydanio rerio (Fish, fresh water)
Exposure period : 48 hour(s)
Unit : mg/l
NOEC : = 500 measured/nominal
LC50 : = 620 measured/nominal
Limit test : no
Analytical monitoring : no
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 1987
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : In the reference by Coulston and Korte, two different concentrations and an average concentration are listed for the lowest lethal concentration (1000, 800 and 800 mg/l, respectively) and the LC50 value (680, 560 and 620 mg/l, respectively). Therefore, it looks like the study was performed in duplicate. However, information about the individual concentrations tested is absent. The average lowest lethal concentration should be 900 mg/l, since the average of 1000 and 800 mg/l is 900 mg/l.

Result : The only data mentioned in the Freitag et al. study were the highest concentration without effect (500 mg/l), the lowest lethal concentration (800 mg/l) and the LC50 value (620 mg/l).

Source : PCA Services, Inc Durham, NC

Test condition : The test was performed in a closed system. The volume of the vessels was not stated. Eight liters of water were added to the vessels (type of water used was not stated), and the water was aerated for one hour. Test material was then added (concentrations were not stated). Twelve fish were placed in each test container (numbers of containers were not listed). The pH and the concentrations of oxygen were determined at 0, 24 and 48 hours. The concentrations of test material at these time points were measured using HPLC. The study was terminated at 48 hours. The LC50 values at 48 hours were determined graphically by plotting the mortality in percent against the concentration on probability paper. No other information about test conditions was mentioned.

Reliability : (2) valid with restrictions
OECD Guideline test; however the test method was not described in detail. Raw data were not provided. The purity of the material is unknown.

07.01.2004 (19) (17)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 24 hour(s)

Unit	:	mg/l
NOEC	:	= 62.5 measured/nominal
EC50	:	= 290 measured/nominal
Limit Test	:	no
Analytical monitoring	:	no data
Method	:	OECD Guide-line 202
Year	:	1987
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The highest concentrations without effect (NOEC) in both experiments were 75 and 50 mg/l, the lowest concentration that caused inhibition (LClo) was 900 mg/l (both replicates) and the EC50 values were 270 and 310 mg/l. The average NOEC, LClo and EC50 values were listed as 75 (the actual value of the average is 62.5), 900 and 290 mg/l. The 95% confidence limits for the two replicates were 213-343 and 229-420, respectively. The chi squared values for the two replicates were 2.60 and 10.96, respectively. Information about the individual concentrations tested is absent. There was no information listed about water quality parameters, dissolved oxygen and pH.
Source	:	PCA Services, Inc Durham, NC
Test condition	:	Groups of 10 daphnia (between 6 and 24 hours old) were exposed to increasing concentrations of the test material for 24 hours. The tests were carried out in duplicate, and the test containers were kept in the dark. Concentrations tested were not mentioned. Negative controls were also tested. After 24 hours, the number of immobilized daphnia (showing no movements within 15 seconds after gentle agitation of the test container) was determined. The control experiments had to show less than 10% immobility. The EC50 value at 24 hours was determined by graphically plotting the immobilization against the concentration on probability paper. When possible, the statistical analysis (with confidence limits of 95%) was performed according to the method of Litchfield and Wilcoxon. No additional information about the method was listed.
Reliability	:	(2) valid with restrictions Test was a guideline study. However, few details were present. No raw data were listed. Concentrations of test material did not appear to be measured analytically and closed systems were not used. Therefore, some of the material may have volatized
Flag	:	Critical study for SIDS endpoint

07.01.2004 (19) (17)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	= 1088 measured/nominal
Limit test	:	no
Analytical monitoring	:	no data
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	1987
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The EC50 value listed above is for 72 hours (although the study was conducted for 96 hours). Results for 96 hours were not listed.
Result	:	The percentage of growth inhibition with respect to control for 500, 700, 1000, 1400 and 1875 mg/l test material for the first replicate was 27.7%,

22.9%, 43.6%, 78.3% and 82.8% The percentage of growth inhibition with respect to control for 500, 700, 1000, 1400 and 1875 mg/l test material for the second replicate was 8.5%, 29.0%, 45.2%, 65.4% and 80.2%. The 72 hour EC50 values were 1075 and 1100 mg/l for the two replicates. The average was 1088 mg/l.

Source : PCA Services, Inc Durham, NC

Test condition : The study was performed in closed containers to limit volatization of the test material. The algae used in the study came from a continuously irradiated algal culture. The air space of the closed test containers and aeration with CO2 -enriched air were optimized in such a way that the growth of the algae in the closed containers was equal to growth that would occur in open test vials.

The algae were suspended in a nutrient solution, continuously irradiated and exposed to increasing concentrations of test material (0, 20, 30, 40, 60, 90 and 120 mg/l) in duplicate. During the experiment, the containers were gently agitated to avoid sedimentation of the algae. The concentration of the algae was determined by measurement of the extinction (wavelength was not indicated) after 0, 24, 48, 72 and 96 hours. The percentage of inhibition was calculated according to the formula mentioned in the guideline. The EC50 values at 72 and 96 hours were determined graphically by plotting the linear percentage of growth inhibition against the logarithm of the concentration.

Reliability : (2) valid with restrictions
Test was a guideline study. However, few details were present. Concentrations of test material did not appear to be measured analytically

Flag : Critical study for SIDS endpoint

07.01.2004 (19) (17)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo	:	In vivo
Type	:	Toxicokinetics
Species	:	rat
Number of animals		
Males	:	10
Females	:	0
Doses		
Males	:	154 ppm (344 dpm/mL)
Females	:	
Vehicle	:	
Route of administration	:	inhalation
Exposure time	:	6 hour(s)
Product type guidance	:	
Decision on results on acute tox. tests	:	
Adverse effects on prolonged exposure	:	
Half-lives	:	1st: 2nd: 3rd:
Toxic behaviour	:	
Deg. product	:	
Method	:	
Year	:	1982
GLP	:	no
Test substance	:	other TS

Method : The test material was synthesized at a commercial supplier with a specific gravity of 4.10 mCi/mmol. The purity was analyzed to be >99.5%.

Male SD rats were obtained from a commercial supplier, and individually identified by metal ear tag. They were housed in controlled rooms with conditions adequate for the species. They were given a commercial diet and water ad libitum except during inhalation exposures. A minimum of 48 hours prior to exposure, jugular cannulas were implanted.

Inhalation exposures were conducted in 30L whole-body chambers with dynamic airflow conditions. The atmosphere was generated by metering the 2-NP into the airstream. Chamber atmosphere was analyzed every 30 minutes by GC. Rats were exposed for 5.5 hours to 154ppm 1-NP. Two 6-hour exposures were then conducted at 20ppm (4 rats to determine blood and plasma concentration-time profiles, and 6 other rats to define the excretion and tissue distribution of the radioactivity.

Blood samples were collected via the jugular cannula while patent, and through the orbital sinus or tail vein thereafter. Plasma was separated from blood cells and tested for radioactivity.

Exhaled air was trapped by pulling room air through a series of absorbant tubes and analyzed, and urine was collected at 4-hour intervals and feces was collected at 24-hour intervals, frozen, and analyzed as well.

Animals were sacrificed, and the liver, kidney, lung, brain, heart, skeletal muscle, fat, and skin, and a 33% aqueous homogenate of the carcass were oxidized and analyzed by liquid scintillation counting for remaining radioactivity.

Time-weighted average exposure concentrations were calculated. Half-

lives were estimated by least-squares analysis. Where appropriate, the groups were compared using a two-tailed Students' t-test with P<0.05 selected for the criterion of statistical significance.

Result : The major route of excretion was the l ungs (50% of the dose was recovered following the exposures as 14CO2). Data indicate that 40% of the inhaled dose was absorbed. Another 3.7% of the dose was captured via the lungs as unchanged 14C-2NP after the 20ppm exposures, and 21.9% following the 154ppm exposures, the difference attributed to the loss of volatile radioactivity during preparation for analysis. Urine and feces represented minor routes of excretion. The amount of radioactivity eliminated by these routes was roughly proportional to the delivered dose.

The relative distribution of 2-NP in the tissues and the tissue/blood ratios were similar regardless of the dose delivered.

The estimated half-life for 2-NP in the rat is less than 2 hours. 2-nitropropane was a low potential to accumulate in the rat. The kinetics of 2-NP are nonlinear in rats when the exposure concentration is less than 154ppm.

Reliability : (2) valid with restrictions
2 (meets generally accepted scientific methods, well-documented, and acceptable for assessment)

12.04.2005 (21)

In Vitro/in vivo : In vivo
Type : Toxicokinetics
Species : monkey
Number of animals
Males : 0
Females : 2
Doses
Males :
Females :
Vehicle : other: ether/alcohol
Route of administration : dermal
Exposure time : 12 hour(s)
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st.:
2nd.:
3rd.:
Toxic behaviour :
Deg. product :
Method :
Year :
GLP :
Test substance : other TS: 14C-labeled 2-NP

Method : SKIN ABSORPTION
The test material was dermally applied to the shaved backs of 2 female rhesus monkeys. A single dermal dose of the test material was applied to the intact skin. The test site was covered for 12 hours with a foil patch and taped air tight over the test site. The skin was wiped with soap and acetone swabs, and the patch and swabs were examined for radioactivity. Seventy-two hours after the application, the test site was excised. Skin and subcutaneous fat / tissue, blood, urine, and feces were assayed for radioactivity using a liquid scintillation counter. Skin samples were examined histologically.

Result : SKIN ABSORPTION
Neither animal showed any signs of toxicity. Urine and feces output was

very low during the 12 hours immediately post-dosing. Urine output normalized after 12 hours, and feces output normalized after 48 hours. There was no effect of exposure on bodyweights.

Excretion of the total dose of test material was 0.693% in 72 hours, and 96.6% of it was through the urine. Approximately 3.6% was excreted in the feces. Exhaled air was not trapped as part of this experiment.

Blood levels of 2-NP reached a maximum of 39.3 ng after 2 hours, but dropped to essentially zero at 24 hours post-dosing. Excised skin contained 0.3% of the total dose, and 0.001% in the subcutaneous fat and tissue. Approximately 30% of the dose was recovered from the swabs used to wipe the skin after the 12-hour occluded exposure. The high loss of test material (98.2% of the total dose) can be attributed to the high volatility of the material. Absorption of the 2-NP through the skin occurred in very low amounts.

Reliability : (2) valid with restrictions
2 (meets generally accepted scientific standards, well-documented, and acceptable for assessment)

12.04.2005 (22)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	565 - 885 mg/kg bw
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	
Year	:	1960
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method : Methods information is specified to oral administration.
Result : The LD50 was reported to be 725 mg/kg +/- 160 mg/kg.

In-life observations were progressive unsteadiness, weakness, incoordination ending in ataxia. Narcotic action was noted. Liver damage was noted at necropsy.

Reliability : (4) not assignable
documentation insufficient for assessment

12.04.2005 (23)

Type	:	LD50
Value	:	500 - 750 mg/kg bw
Species	:	rabbit
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	
Year	:	1940
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method	:	Rabbits were obtained from a commercial supplier and were evaluated for health prior to study start. Animals were dosed orally by stomach tube with undiluted test material. Animals were fasted for 24 hours to reduce the volume of stomach content. Following administration, the animals were released and observed for 2-2 hours prior to caging.
Result	:	Principle in-life observations noted from 20-40 minutes following dose were: progressive weakness and collapse, unsteadiness, incoordination ending in ataxia, and changes of respiration patterns (slowing, the later increasingly rapid rate). There were no blood findings noted, and no gross changes in the blood.
Reliability	:	(2) valid with restrictions 2e (meets generally accepted scientific standards, well-documented, and acceptable for assessment)

12.04.2005 (24)

Type	:	LD50
Value	:	= .352 - .454 ml/kg bw
Species	:	mouse
Strain	:	CD-1
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other
Year	:	1979
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The 14-day oral LD50 value for CD-1 mice (number and sex were not listed) was 0.4 (0.352-0.454) ml/kg. Based on a density of 0.9821 g/cm3, the value in mg/kg is 393 (346-446).
Source	:	PCA Services, Inc Durham, NC
Reliability	:	(4) not assignable There is not enough information to assign a reliability rating.

12.04.2005 (25)

Type	:	LD50
Value	:	180 - 280 mg/kg bw
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	
Doses	:	no data
Method	:	other: no data
Year	:	1956
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	There are no methods information given in the report, nor any detailed results data. Only the oral LD50 is reported.
Reliability	:	(4) not assignable 4e (documentation on methods is insufficient for assessment)

12.04.2005 (26)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	= 400 - 720 ppm
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	98
Vehicle	:	
Doses	:	367, 405, 461 and 574 ppm (males) and 370, 416, 464, 602 and 805 ppm (females)
Exposure time	:	6 hour(s)
Method	:	other
Year	:	1977
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Males: None of the controls or males exposed to 367 (+/- 6) ppm died. Five males exposed to 405 (+/- 11) ppm died (3 on day 2 and 2 on day 3). Seven males exposed to 461 (+/- 13) ppm died by day 2. All eight males exposed to 574 +/- 28 ppm died within 2 days. Weight gain of survivors did not appear to be affected by treatment. Animals moved about the chambers immediately upon exposure, followed by slight depression and hyperventilation. Cyanosis was observed in animals exposed to concentrations > = 405 ppm. Necropsies were unremarkable. The LC50 value was 400 +/- 38 ppm. Females: None of the controls or animals exposed to 370 +/- 10, 416 +/- 29, 464 +/- 22, or 602 +/- 11 ppm died. Eight out of 10 rats exposed to 805 +/- 37 ppm died within 2 days. Weight gain of animals exposed to concentrations < = 602 ppm did not appear to be affected by treatment. The females that survived exposure to 805 ppm did not gain weight over the course of the study. Animals moved about the chambers immediately upon exposure, followed by slight depression and hyperventilation. Concentrations > = 602 ppm produced cyanosis within 3-6 hours. Necropsies were unremarkable. The LC50 value was 720 +/- 46 ppm.
Source	:	PCA Services, Inc Durham, NC
Test condition	:	Animals: Sprague-Dawley rats (145-194 g) were used in the study. Food and water were supplied ad libitum (except for during exposure, when they were withheld). The test material was vaporized at ambient temperature. Nitrogen was passed through a scintered glass sparger into a tube containing the test material (30 ml) at a variable rate (100-250 cc/min). The stream was admixed with "breathing air" (6.2 liters/min) and passed to a 36.2 liter, glass inhalation chamber. Vapor concentration was monitored continuously using an infrared spectrophotometer. The animals were exposed to test material for 6 hours and observed for a period of 14 days. Concentrations tested in groups of 8 males were 367, 405, 461 and 574 ppm. Groups of 10 females were exposed to 370, 416, 464, 602 and 805 ppm. Groups of control animals (N= 8 for both sexes) were exposed similarly, with the exception that water was substituted for test material in the vaporizer tube. Deaths were recorded daily and signs of toxicity were recorded at unlisted intervals. Survivors were euthanized at 14 days. Necropsies were performed on animals (including those that died prematurely). The LC50 value was estimated using the method of Miller and Tainter (Proc. Soc. Exper. Biol. Med. 57:261, 1944).
Test substance	:	Purity of the material was not listed. The test material was commercial grade. Therefore, it is assumed that it is of fairly high purity.
Reliability	:	(1) valid without restriction The study is comparable to a guideline test.
Flag	:	Critical study for SIDS endpoint

10.02.2004 (27)

Type	:	LC100
Value	:	= 14700 ppm
Species	:	rat
Strain	:	other:unknown
Sex	:	no data
Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	4 hour(s)
Method	:	other
Year	:	1973
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Experiments were also performed with nitromethane, nitroethane and 1-nitro propane. The amount of MetHb found after exposure to these materials was < 1% for nitromethane, 2.8% for nitroethane and 4 -10% for 1-nitropropane.
Result	:	In the first experiment, one rat exposed to 14,700 ppm 2-nitropropane (52 g/m3) died after 4 hours. One rat exposed to 760 ppm for 8 hours on one day survived exposure and was killed immediately afterwards. Another rat exposed to 760 ppm for 8 hours was allowed to recover, but died 48 hours later. The two rats that were exposed to 760 ppm for 8 hours a day for two days died 2 hours after the end of the second session. The 5 rats exposed to 80 ppm for 8 hours/day for 5 days survived. The methemoglobin concention in blood of the rat exposed to 14,700 ppm was 84%. 2-nitropropane (23 mg/100 g) was found in the liver of this animal. 2-nitropropane (18 mg/100 g) was also found in the liver of animals exposed to 760 ppm. The treatment that corresponded to this concentration was not listed. No 2-nitropropane was found in the liver and no methemoglobin was found in the blood of animals exposed to 80 ppm.
Source	:	PCA Services, Inc Durham, NC
Test condition	:	Wistar rats (avg. weight 250 g) were exposed by inhalation to 80 (N=5), 760 (N=4) or 14700 (N =1) ppm 2-nitropropane for 8 hours/day for 5 days, 8 hours/day for 1 or 2 days, and 4 hours on one day, respectively. Concentrations were confirmed by gas chromatography. Methemoglobin concentrations in blood and test material concentrations in the liver, lung, heart and kidney were measured.
Reliability	:	(2) valid with restrictions The study was performed before GLP. Little information is provided about study animals or test conditions.

06.02.2004 (28)

Type	:	LC50
Value	:	= 558 - 560 ppm
Species	:	mouse
Strain	:	ICR
Sex	:	male/female
Number of animals	:	55
Vehicle	:	
Doses	:	454, 558 and 738 ppm (males) and 495, 640 and 740 ppm (females)
Exposure time	:	6 hour(s)
Method	:	other
Year	:	1977
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Males: None of the controls or males exposed to 454 (+/- 8) ppm died.

Seven males exposed to 558 (+/- 12) ppm died (4 on day 7 and 3 between days 7 and 14). Nine males exposed to 738 (+/- 25) ppm died (1 on day 2, 2 on day 3 and 6 between days 3 and 7). Animals gained 4-6 grams during the study. Animals moved about the chambers immediately upon exposure, followed by slight depression and hyperventilation. Cyanosis was observed in animals exposed to 558 and 738 ppm. Necropsies were generally unremarkable, but some petechial hemorrhage of the lung was noted. The LC50 value was 558 +/- 123 ppm.

Females: None of the controls died. Two females exposed to 495 ppm died (on days 3 and 7). Eleven females exposed to 640 ppm (no standard error was listed) died by day 7. Three of these animals died by day 3. All 14 females treated with 740 ppm died within 14 days (5 died within 3). Animals exposed to 640 or 495 ppm did not gain weight. However, controls only gained 0.7 g (compared to 6.0 g in males). Animals moved about the chambers immediately upon exposure, followed by slight depression. Cyanosis was observed at 640 and 740 ppm. Necropsies were generally unremarkable. The LC50 value was 560 +/- 30 ppm.

Source : PCA Services, Inc Durham, NC

Test condition : Animals: ICR mice (19-23 g) were used in the study. Food and water were supplied ad libitum (except for during exposure, when they were withheld).

The test material was vaporized at ambient temperature. Nitrogen was passed through a scintered glass sparger into a tube containing the test material (30 ml) at a variable rate (100-250 cc/min). The stream was admixed with "breathing air" (6.2 liters/min) and passed to a 36.2 liter, glass inhalation chamber. Vapor concentration was monitored continuously using an infrared spectrophotometer.

The animals were exposed to test material for 6 hours and observed for a period of 14 days. A group of control animals was exposed similarly, with the exception that water was substituted for test material in the vaporizer tube. Deaths were recorded daily and signs of toxicity were recorded at unlisted intervals. Animals were weighed at the beeginning of the study and at termination on day 14. Necropsies were performed on animals (including those that died prematurely). The LC50 value was estimated using the method of Miller and Tainter (Proc. Soc. Exper. Biol. Med. 57:261, 1944).

Test substance : Purity of the material was not listed. The test material was commercial grade. Therefore, it is assumed that it is of fairly high purity.

Reliability : (1) valid without restriction
The study is comparable to a guideline test.

06.02.2004 (27)

Type : LC50
Value : 12.07 - 14.43 mg/l
Species : rat
Strain : Wistar
Sex : female
Number of animals :
Vehicle :
Doses :
Exposure time : 1 hour(s)
Method :
Year : 1957
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : The test material was evaluated at various (unspecified) concentrations to evaluate the LC50 for 2-NP.

Result : Irritation of the nasal and conjunctival membranes was severe, followed by

irritibility, ataxia, increased respiration, and eventual respiratory collapse. If animals are removed from exposure prior to terminal stage, good recovery is obtained and normality returns within 24 hours, with the exception of mucous membrane irritation, which persists for approximately 4 days.

Reliability : (4) not assignable
4 (documentation insufficient for assessment)

13.04.2005 (29)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 2000 mg/kg bw
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	2000 mg/kg
Method	:	other
Year	:	1982
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Result : None of the animals died or exhibited signs of toxicity. The treated skin sites did not exhibit any erythema or edema after 24 hours of treatment. Body weight gains were normal. Gross necropsies of the animals were normal.

Source : PCA Services, Inc Durham, NC

Test condition : Animals: The animals were at least 9 weeks old and weighed 2.6 +/- 0.3 kg. They were acclimated for 7 days before use. Twenty four hours before the test, each animal was examined. Only animals with no skin injury were used. The animals were given food and tap water ad libitum.

Test material: The test material was used as supplied.

Test conduct: The abdomens of all animals were shaved free of hair, and the abdominal skin was abraded. The abrasions were made with a blunt hypodermic needle (without producing bleeding) and were placed 2 -3 cm apart. Test material (2000 mg/kg, 4,4 - 5.7 ml) was spread over the shaved area of all rats. The skin area was then covered with gauze and a sheet of impervious rubberized cloth. The trunk was further enclosed with a flexible stainless steel protective screen held in place by tape. The dressings were removed after 24 hours. The sites were cleaned and examined for erythema and edema. The animals were observed for toxicity over 14 days. Body weights were recorded prior to application of material and at 7 and 14 days. Gross necropsies were performed on all rabbits euthanized on day 14.

If possible, the LD50 value, slope and 95% confidence limits were calculated using the probit analysis of Finney (Cambridge Press, 1979) adapted to a BASIC computer program.

Test substance : An analytical report submitted with the sample indicated that the purity of the test material was 97.10%. The test material also contained (by weight) 1.01% nitroethane, 2.59% 1-nitropropane and 0.023% water.

Reliability : (1) valid without restriction
The study is comparable to a guideline study.
The study was comparable to a guideline, limit study.

06.02.2004 (30)

Type	:	LD50
Value	:	> 200 mg/kg bw
Species	:	rabbit
Strain	:	
Sex	:	
Number of animals	:	10
Vehicle	:	
Doses	:	200 mg/kg
Method	:	
Year	:	1956
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method	:	2-NP was applied to the skin of 10 rabbits at a dose of 200 mg/kg.
Result	:	"...a dose of 200 mg/kg are not absorbed in toxic amounts".
Reliability	:	(4) not assignable

12.04.2005 (26)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	not irritating
Classification	:	
Method	:	other
Year	:	1982
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Result	:	All erythema and edema scores at 24 and 72 hours were 0. The material was not irritating.
Source	:	PCA Services, Inc Durham, NC
Test condition	:	The test was conducted in six albino rabbits weighing 2.4 +/- 0.1 kg. The skin from the back area of each animal was clipped free of hair. The skin site left of the middorsal line on each rabbit was left intact and the skin on the right side was abraded at 2 sites with a blunt hypodermic needle. The abrasions went through the stratum corneum but did not disturb the derma or produce bleeding. A total of 4 sites (2 intact and 2 abraded) were tested per animal. A 0.5 ml sample of test material was applied to each site and covered with a moistened gauze pad. The entire trunk was then wrapped with a rubberized, impervious cloth and a flexible stainless steel wire screen held in place by tape. The dressings were removed after 24 hours and the treated skin sites were gently cleaned. The skin reactions were scored immediately (24 hr) and 48 hours later (for a total of 72 hours). The irritation index for each rabbit was calculated as a sum of all the scores divided by 4.
Test substance	:	A certificate of analysis supplied with the report indicated that the purity of the test material was 97.10%. The test material also contained (by weight) 1.01% nitroethane, 2.59% 1-nitropropane and 0.023% water.

Reliability	:	(1) valid without restriction The study is comparable to a guideline study.
12.04.2005		(31)
Species	:	rabbit
Concentration	:	undiluted
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	not irritating
Classification	:	
Method	:	
Year	:	1940
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Animals were shaved over the anterior abdominal wall. The test material was applied to the animal held in a supine position. The test material was allowed to evaporate, and when dry, the animal was released. The treatments were repeated daily until 5 treatments had been made.
Result	:	There was no illness or external signs of toxicity or irritation noted.
Reliability	:	(2) valid with restrictions 2 (meets generally accepted scientific standards, well-documented, and acceptable for assessment)
12.04.2005		(24)
Species	:	rabbit
Concentration	:	undiluted
Exposure	:	no data
Exposure time	:	
Number of animals	:	1
Vehicle	:	
PDII	:	
Result	:	slightly irritating
Classification	:	
Method	:	
Year	:	1956
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The test material was placed on the intact or abraded skin of a rabbit, and scored by the method of Draize.
Result	:	The test material produced an insignificant degree of irritation on the intact or abraded skin.
Reliability	:	(4) not assignable
12.04.2005		(26)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	72 hour(s)
Comment	:	
Number of animals	:	6
Vehicle	:	none
Result	:	slightly irritating

Classification	:	
Method	:	other
Year	:	1989
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The maximum eye irritation score was 1.0 +/- 1.7 at 24 hours. At 48 hours, the mean score was 0.3 +/- 0.8. This is consistent with a classification of "minimally irritating to eyes". The incidence of positive ocular responses in all animals was 0. Scores for conjunctival redness and chemosis, corneal opacity and effects on the iris were not listed. According to the protocol, a corneal opacity score of 1 was considered to be a positive response, but conjuctival redness, chemosis and discharge scores of 1 were not. Since no positive responses were noted in any of the animals, it is likely that the minimal effects observed in some eyes were limited to the conjunctiva. According to 16 CFR Part 1500, 2-nitropropane was not considered a primary irritant. The untreated eyes of all animals appeared normal at all observations.
Source	:	PCA Services, Inc Durham, NC
Test condition	:	Six young adult New Zealand White rabbits weighing 2-3 kg were acclimated for at least 5 days before use. Food and water were supplied ad libitum. Eyes were examined with sodium fluorescein and a slit light equipped with a cobalt blue filter prior to dosing to verify the absence of pre-existing ocular lesions. The test material (0.1 ml) was instilled into the right conjunctival sac of each rabbit and the lids were held together for one second and released. The animals were observed twice daily for mortality at least 5 hours apart. Primary eye irritation was evaluated 24, 48 and 72 hours after the test material was administered. The cornea, iris and conjunctiva were scored separately according to the method of Draize. The test was considered positive if four or more of the animals had a positive reaction. If only one animal was affected, the test was negative. If two or three animals were affected, the test was to be repeated. The second test was to be considered positive if 3 or more animals had a positive reaction. If one or two animals were affected, the test was to be repeated again. If any animal in the third test had a positive reaction, the material was regarded as an irritant.
Test substance	:	The test material was used as supplied by WR Grace and Company.
Reliability	:	(2) valid with restrictions Purity of the material is unknown.

12.04.2005 (32)

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	
Comment	:	
Number of animals	:	6
Vehicle	:	
Result	:	slightly irritating
Classification	:	
Method	:	other: Federal Register, Title 21, Pt. 191, para.191.12
Year	:	1974
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The test material (0.1mL) was instilled into the lower eye lid of the righ eye of each of 6 albino rabbits. After introduction of the test material, the eyelid was held closed for 1 second. The test animals were maintained without

		further treatment, and their eyes were examined at 24, 48, and 72 hours following treatment. Examination of the eyes was aided by use of a hand-held slit lamp and spectacle loupes. After the 24-hour examination, a drop of fluorescein sodium opthalmic solution was placed into each eye to aid in the visualization of damage to the cornea. Responses of the eye were graded by the Draize technique.
Result	:	There was no indication of ulceration or other surface lesions which were detected following instillation of fluorescein solution. Eyes of a few rabbits showed signs of moderately excessive lacrymation at the 48- and 72-hour examinations.
Reliability	:	(2) valid with restrictions 2e (meets generally accepted scientific standards, well-documented, and acceptable for assessment)

12.04.2005 (33)

Species	:	rabbit
Concentration	:	undiluted
Dose	:	
Exposure time	:	
Comment	:	
Number of animals	:	1
Vehicle	:	
Result	:	slightly irritating
Classification	:	
Method	:	
Year	:	1956
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Undiluted test material was placed in one eye of one rabbit.
Result	:	The test material produced an insignificant degree of irritation in the eye of the one rabbit tested.
Reliability	:	(4) not assignable documentation insufficient for assessment

12.04.2005 (26)

5.3 SENSITIZATION

Type	:	Intracutaneus test
Species	:	guinea pig
Concentration	:	1st: Induction 1 % intracutaneous 2nd: Challenge 1 % intracutaneous 3rd:
Number of animals	:	30
Vehicle	:	
Result	:	not sensitizing
Classification	:	
Method	:	other
Year	:	1982
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	During the induction phase, the first 3 injections of a 5% solution of test material caused necrosis. Therefore, the last seven injections were made with 1%. Whether or not any reactions were observed at this concentration was not listed. Positive control animals exhibited necrosis during the entire induction period.

None of the animals that were induced with test material reacted after challenge with the test material. In the positive control group, 8/10 animals challenged with 0.03% DNCB and all animals challenged with 0.3% DNCB had skin reactions at 24 hours. At 48 hours, all positive control animals injected with 0.3% DNCB and none of the positive controls injected with 0.03% DNCB had positive reactions. All negative controls challenged with 0.3% DNCB had skin reactions at 24 and 48 hours, and none of the negative controls challenged with 0.03% DNCB had skin reactions at 24 and 48 hours.

Source : PCA Services, Inc Durham, NC

Test condition : Thirty male guinea pigs (250-300 g) were divided into 3 groups of 10 each. The animals' backs and flanks were shaved free of hair. One group was intradermally injected with 0.05 ml of a 5% solution of test material in saline. The second group (positive control) was similarly injected with 0.05 ml of a 0.3% dinitro-chlorobenzene (DNCB) solution that was solubilized in a minimum volume of alcohol and made to volume with saline. The third group (negative control) was injected with 0.05 ml of saline. After 24 hours, the injected sites were scored for erythema and edema according to the method of Draize (Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics, Association of Food and Drug Officials of the United States, p.48, 1957). At 48 hours the animals were again injected with 0.1 ml of their respective solutions. The injections were repeated 2-3 times a week until 10 injections were made. Since necrosis was noted after two injections with 5% test material, the last 7 injections were made with 1% solution.

The animals were allowed to rest for 2 weeks after the last injection. On the first day of the third week (or the 42nd day after the first injection), the animals in each group were challenged intradermally with 0.1 ml of solution at a new site. Animals from the first, second and third groups were challenged with 1% test material, DNCB solution (0.03% and 0.3%), and test material and both DNCB solutions (at different sites), respectively. After 24 hours, the injected sites were depilated with "Nair". The injected sites were scored for erythema and edema 3 hours after hair removal. The sites were rescored at 48 hours.

The test material was considered a sensitizer if the number of animals exhibiting skin reactions was higher in Group 1 than in the negative control group. The positive control group was an internal control for the test.

Test substance : The analytical report submitted with the sample indicated that the purity of the test material was 97.10%. The test material also contained (by weight) 1.01% nitroethane, 2.59% 1-nitropropane and 0.023% water.

Reliability : (1) valid without restriction
The study was comparable to a guideline study.

06.02.2004 (34)

5.4 REPEATED DOSE TOXICITY

Type : Sub-chronic
Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : up to 6 months
Frequency of treatm. : 7 hours/day, 5 days/week
Post exposure period :
Doses : 27 or 207 ppm
Control group : yes

NOAEL	:	= 27 ppm
LOAEL	:	= 207 ppm
Method	:	other
Year	:	1977
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Remark : The study was conducted at the Huntingdon Research Center under NIOSH contract No. 210-75-0039.

The material nitromethane was tested concurrently (at 98 and 745 ppm) in this study. This material had no effect on the pathology of the liver. 2-nitropropane also was tested in rabbits at the same concentrations. Rabbits and rats were exposed in the same chambers. The results for the rabbit study are described in a different summary.

The 6-hr LC50 value also was determined, using rats of both sexes. In males, this value was approximately 400 ppm. Females were less sensitive, as none died after exposure to a concentration that killed all of the males (580 ppm).

The high dose for the study was originally 400 ppm (instead of 200 ppm). However, since excessive mortality occurred within 3 days, the exposure was stopped. New groups of rats with average weights of 96 g were then exposed to 200 ppm (nominal). These animals weighed less than controls or rats exposed to 27 ppm (avg. weight 171 g). Therefore, results for rats exposed to 207 ppm were compared to those of controls that had significantly higher weights. A new control group comprised of rats with weights approximating those of rats exposed to 207 ppm should have been added when animals were exposed to 207 ppm.

The authors noted that some of the material may have decomposed during the vaporization process, which was conducted at 75-120 degrees C. Therefore, the possibility exists that a decomposition product contributed to the toxicity.

Since food and water were not withdrawn during exposure, it is possible that some of the material was ingested.

The NOAEL for this study was 27 ppm. Increased wet/dry lung weights that occurred at 3 months were not supported by histologic evidence of edema.

Result : The average (+/- SD) concentrations of test material in the exposure chambers were 27.2 +/- 3.1 ppm and 207 +/- 15 ppm for the nominal concentrations of 25 and 200 ppm, respectively.

Effects at 207 ppm: There was no effect of treatment on body weight. Hematocrit, hemoglobin, red blood cells and prothrombin time were decreased at 10 days and 1 month in rats exposed to 207 ppm. At three months, the prothrombin time of rats exposed to 207 ppm was decreased and red blood cells were increased. Methemoglobin concentrations were increased at 6 months. None of the hematologic changes were considered by the authors to be related to exposure. Serum glutamic-pyruvic transaminase was increased in rats exposed to 207 ppm at 10 days and 1 and 6 months. Serum throxin was increased in rats exposed to 207 ppm at 3 months. Wet/dry weights of lungs were increased in rats exposed to 207 ppm for 1, 3 or 6 months. Relative lung and liver weights of animals exposed to 207 ppm test material were elevated at 3 and 6 months. At 1, 3 and 6 months, rats exposed to 207 ppm had an increased incidence dark hemorrhagic foci in the lungs. The livers of rats exposed to 207 ppm for 3 months had areas of necrosis and surface lesions and were paler in color than controls. After 6 months of exposure to 207 ppm, the livers were

enlarged and pale with numerous masses and lesions.

No exposure-related microscopic alterations were seen in any of the tissues of rats exposed for 2 or 10 days, or 1 month. In all 9 rats euthanized after exposure to 207 ppm test material for 3 months, numerous focal areas of hepatocellular hypertrophy were noted. The hepatocytes in these foci were more eosinophilic than the surrounding cells and usually contained large, vesiculated nuclei. In 4 of the 9 rats, basophilic foci containing hyperplastic, small hepatocytes with hyperchromatic nuclei were observed. Occasionally, mitotic figures were present.

Multiple hepatocellular carcinomas and numerous neoplastic nodules were present in the livers of all 10 rats exposed to 207 ppm test material for 6 months. In many cases, the normal hepatic parenchyma was destroyed. The neoplasms were composed of anaplastic hepatocytes, sometimes forming broad sheets or trabeculae several cells thick. Blood-filled cysts were occasionally seen in the neoplasm. Mitotic figures were commonly observed. The carcinomas appeared to be rapidly growing. However, no metastatic hepatocellular carcinomas were seen in any of the other tissues examined.

Effects at 27 ppm : There was no effect of treatment on body weight. Hematocrit and red blood cells were decreased and methemoglobin was increased at 10 days in rats exposed to 27 ppm. Hematocrit also was decreased at 1 month in rats exposed to 27 ppm. Rats exposed to 27 ppm for 3 months had increased hematocrit, hemoglobin and red blood cells. Methemoglobin concentrations were increased at 6 months. None of the hematologic changes were considered by the authors to be related to exposure. Wet/dry weights of lungs were increased in rats exposed to 27 ppm for 3 months. No exposure-related macroscopic or microscopic changes were observed in any organ that was examined.

Source : PCA Services, Inc Durham, NC

Test condition : Animals: Two hundred fifty male, Sprague-Dawley rats (100 g) were acclimated for 14 days. All animals were allowed food and tap water ad libitum. The animals were randomly allocated to 25 groups of 10 animals each.

Generation of vapor: Test material was pumped at a constant flowrate to the vaporization apparatus. Vaporization was accomplished by utlizing a counter-current flow of heated air. The temperatures at the top and bottom of the column were 75 and 120 degrees C, respectively. Air flows were within 18-25 l/min. The concentrated vapor-air mixture was piped to the exposure chamber inlet and diliuted with air flowing at approximately 1000 l/min. The volume of the exposure chambers was 6 cubic meters. Air was supplied by an air conditioning system separate from the general laboratory system. It was controlled for both temperature (21.5 degrees C) and relative humidity (50%. Chamber flowrate was monitored as the pressure drop across a sharp-edged orifice.

Rats were housed in the chambers 24 hours/day. They were caged (10/cage) in wire mesh stainless steel cages, with a dropping pan beneath. Once per day (just prior to exposure) animals were removed from the chambers and all pans and the chamber interiors were hosed down with hot water and a disinfectant. All cages were exchanged for clean ones once per week.

Each chamber was autosampled approximately every hour for concentration of test material. The samples were analyzed using a calibrated Wilks MIRAN I infrared absorption spectrophotometer (at a wavelength of 3.4 microns). Chamber concentrations were read from the

charts twice daily. Nominal concentrations were obtained by noting the volume of compound used during the each day.

Study conduct: Groups of 10 animals were exposed to 25 or 200 ppm (nominal) test material and euthanized at 2 days, 10 days, 1 month, 3 months or 6 months. Animals were weighed at unlisted intervals. Average weights of controls and rats exposed to 27 ppm were 171 g at time of exposure. Blood for hematolgic (hematocrit, hemoglobin, erythrocyte count, prothrombin time and methemoglobin) and biochemical (serum glutamic-pyruvic transaminase, ornithine carbamyl transferase and thyroxin) analyses was obtained from the abdominal aorta at each termination. All animals that died or survived to termination were given complete necropsies. The liver, kidney, thyroid, lungs plus trachea (both wet and dry) and brain (both wet and dry) were weighed. The lungs, adrenals, bronchi, cerebellum, cerebral hemispheres, eyes, kidneys, liver, spleen, thyroid and trachea were processed and evaluated microscopically.

Statistical analyses: Data were first evaluated for homogeneity using Bartlett's test, with the rejection level set at p = 0.01. A one-way analysis of variance was then conducted (with the critical value set at p = 0.10). Data that were significantly different were then analyzed with the Student's t-test to determine which means were significantly different from control. The critical value for these analyses was P = 0.05.

Test substance : Purity of the test material was 94.45 % (by weight). It also contained 3.07% 1-nitropropane, 1.96% nitroethane, 0.42% 2-nitro-2-methylpropane, 0.03% 2-nitrobutane and < 0.01% water. Other minor impurities were not listed.

Reliability : (2) valid with restrictions
Some biochemical and histological analyses that are performed in guideline studies were not conducted. Some of the test material may have been ingested. Animals may have been exposed to a decomposition product. Weights of high dose animals were significantly less than controls.

13.02.2004 (35) (36)

Type : Chronic
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : up to 18 months
Frequency of treatm. : 7 hours/day, 5 days/week
Post exposure period : up to 9 months exposure for some rats followed by 9 months of recovery
Doses : 100 ppm
Control group : yes
NOAEL : < 100 ppm
LOAEL : = 100 ppm
Method : other
Year : 1983
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : It is not known whether the incidences of tumors and other histochemical lesions are for main study and recovery animals or just for main study animals. Appendices that listed incidences of lesions were not included with the report.

Result : Main test animals: Males exposed for up to 12 months and females exposed for up to 18 months had similar body weights as controls. Males exposed for 18 months had lower body weights than controls. Absolute and relative weights of the liver were increased in males treated for 9, 12 or 18 months. Liver weights of exposed females were similar to control. There was no effect of treatment on kidney or brain weight. Serum glutamic-

pyruvic transaminase was increased in males exposed for 18 months (78 +/- 97 U/l compared to 17 +/- 13 U/l in control). There was no effect of treatment on any hematological or any other biochemical parameter. Hepatic lesions were observed in males exposed for 9, 12, or 18 months, with the frequency increasing with length of exposure (6/16, 5/10 and 22/23, respectively). Hepatic lesions were also found in 11/16 males found dead or moribund. Hepatic lesions were also noted in 1/20 females exposed for 9 months and 2/30 exposed for 18 months. None of the 5 females that were found dead or moribund had liver lesions.

Recovery animals: Body weights of males exposed for 3 months and allowed to recover for 15 months and of females in all recovery groups were similar to controls. Males exposed for 6 or 9 months and allowed to recover for 12 or 9 months (respectively) had reduced body weights compared to controls. Absolute and relative weights of the liver were increased in males treated for 3, 6 or 9 months and then allowed to recover. Serum glutamic-pyruvic transaminase was higher in males exposed for 9 months and allowed to recover for 9 months (397 +/- 627 U/ml) than in males exposed for 18 months. Serum ornithine carbamyl transferase values for the 9 month treatment/9 month recovery males (1.12 +/- 1.19 U/ml) appeared to be slightly higher than control (0.55 +/ - 0.28 U/ml). Methemoglobin may also have been elevated in this group (35.6 +/- 12.4 mg/dl in exposed vs. 20.5 +/- 11.4 mg/dl in control). There was no effect of treatment on any hematological or biochemical parameter in females. Hepatic lesions were observed in males exposed for 3, 6, or 9 months that were allowed to recover in similar frequency (6/10, 7/10 and 7/10, respectively). Lesions were also found in livers of 2/10 females in the 9 month treatment/9 month recovery group.

Pathology report:
Neoplasms: The total number of tumors in the unexposed group (43) exceeded the total number of tumors in the exposed group (25). The total number of animals with tumors in the control group (38) also was greater than the exposed group (23). The types of tumors observed in exposed and control females were similar. The most common benign and malignant tumors in control and exposed females were pituitary adenoma and mammary gland adenocarcinoma, respectively. The types of tumors observed in exposed and control males were different. The most common benign and malignant tumors in control males were pituitary adenoma (N= 6) and fibrosarcoma of the skin and sucutis (N = 1). In exposed males the most common benign tumor also was pituitary adenoma (N= 1). However, the most common malignant tumor in exposed males was hepatocellular carcinoma (N=7).

Non-neoplastic pathology: There was an increase in renal calcification in exposed males and females compared to controls. Focal necrosis, vacuolar degeneration and nodular hyperplasia were increased in exposed males and females.

Source : PCA Services, Inc Durham, NC

Test condition : Animals: Two hundred fifty CRL: COBS CD SD BR rats per sex were used in the study. The initial weights and ages were not listed. Rats were acclimated for an unlisted amount of time. All animals were allowed free access to food and water (except during exposure, when food and water were withheld from both controls and exposed animals). The animals were randomly allocated to an exposure group of 125 animals/sex and a control group of 125 animals/sex.

Generation of vapor: Vapors were generated by bubbling purified nitrogen through the test material in an all-glass vessel maintained in a thermostatted water bath (45 degrees C). The test material in the generator was maintained at a constant level. After each week of

operation the remaining test material was discarded and replaced with fresh material. Analyses of the test material remaining after one week showed that the material did not decompose. The effluent from the vapor generator was injected into a section of the chamber containing a large circulating fan that mixed the effluent with air from the inatake air duct. An exhaust blower was operated at a velocity sufficient to provide 15 air changes/hour.

Concentrations of vapors in the exposure chambers were monitored by frequent sampling. Routinely, at least 3 air samples were obtained daily by means of an air-sampling pump operated with a limiting orifice to control flow rate The air from the chamber was withdrawn through two glass impingers aligned in series, filled with ethyl acetate, and immersed in an ice bath. Studies demonstrated that approximately 99% of the test material was trapped in the first impinger. After a suitable sampling period, the contents of the impingers were transferred to a volumetric flask and a known quantity of 1-nitropropane was added as an internal standard. After dilution to volume, an aliqout was injected into a gas chromatograph and compared with standards. The mean concentration of test material was 100 +/- 3ppm. This was equivalent to 312 mg/m3.

Study conduct: Groups of 125 animals/sex were exposed to 100 ppm, 7 hours/day, 5 days/week in 8 x 8 x 12 foot chambers. The control group was housed in a room having environmental conditions similar to those in the exposure chamber. All animals were observed daily for signs of toxicity.

Ten animals per sex per group were euthanized at the following intervals: one month, 3 months, 6 months, 9 months and 12 months. Sixty two and 67 control males and females (respectively) were euthanized at 18 months. Twenty three and 30 exposed males and females (respectively) were euthanized at 18 months. Additional groups of 7 males and 10 females, 8 males and 10 females and 7 males and 8 females were exposed to test material for 3, 6 of 9 months (respectively) and euthanized at 18 months.

Body and liver, kidney and brain weights were obtained at termination. Blood for hematolgic (hemoglobin, erythrocyte count, white blood cell count, prothrombin time, hematocrit and methemoglobin) and biochemical (serum glutamic-pyruvic transaminase, ornithine carbamyl transferase, thyroxin, and triiodothyronine) analyses was obtained from the animals at termination.

All animals that died or survived to termination were given complete necropsies. Special attention was given to the liver and the incidence of tissue masses and nodular appearance was noted. Specimens of lung, liver, kidney, lymph node and any unusual lesions were obtained from each of the rats and processed for histological examination.

Test substance : Purity of the test material was 95.65 % (by weight). It also contained 3.63% 1-nitropropane, 0.20% nitroethane, 0.51% 2-nitro-2-methylpropane and 0.01% water.

Reliability : (2) valid with restrictions
Data were not analyzed statistically. Only one concentration was tested. Some biochemical and histological analyses that are performed in guideline studies were not conducted.

13.02.2004 (37) (38)

Type : Chronic
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation

Exposure period	:	22 months
Frequency of treatm.	:	7 hours/day, 5 days/week
Post exposure period	:	
Doses	:	25 ppm
Control group	:	yes
NOAEL	:	< 25 ppm
LOAEL	:	= 25 ppm
Method	:	other
Year	:	1980
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark : The authors did not consider any of the changes in body weight, serum chemistry or hematology to be related to exposure due to variation of controls and no apparent relationship of the changes to duration of exposure.

The authors considered the NOAEL in this study to be 25 ppm. However, there was a small increase in the incidences of focal vacuolization and liver congestion in exposed males. Since the results were not broken down by length of exposure or duration of recovery, it is difficult to determine whether these increases were due to exposure and/or were reversible.

Result : Main study animals: Body and liver weights of females exposed to test material for 6, 12 or 22 months were significantly greater than control ($p < 0.01$). When expressed on a relative basis, liver weights of females were not elevated. Both relative and absolute liver weights of males exposed for 22 months were significantly greater than control ($p < 0.01$). Relative liver weights of males exposed for 6 months also were greater than control ($p < 0.05$). Absolute weights of kidneys of females exposed for 1 month and males exposed for 12 months were significantly greater than control ($P < 0.05$). Relative kidney weight data were not presented. There was no effect of treatment on brain weight. There was no effect of treatment on serum glutamic-pyruvic transaminase. Ornithine carbamyl transferase activity was increased ($p < 0.05$) in males exposed for 12 months and decreased in males exposed for 3 or 6 months ($p < 0.01$ and 0.05, respectively). Females exposed for 12 months had decreased serum thyroxin ($p < 0.01$). However, day-to day variations in thyroxin in control animals were greater than the difference between the treated and control animals. Hemoglobin and hematocrit were increased in males exposed for 12 months ($p < 0 .01$ and 0.05, respectively). Hematocrit was increased in females exposed for 6 or 12 months ($p < 0.05$ and 0.01, respectively). Erythrocyte and white blood cell counts were increased in males exposed for 6 months ($p < 0.01$). Erythrocyte counts were increased in females exposed for 12 months ($p < 0.05$). There was no effect of treatment on prothrombin time.

Recovery animals: Body weights of females exposed to test material for 3 months and allowed to recover for 19 months were significantly greater than control ($p < 0.01$). There was no effect of treatment on kidney or brain weight. Females exposed for 3 or 12 months and then allowed to recover to 22 months had increased serum thyroxin ($P < 0.01$). Methemoglobin was increased in females exposed for 12 months and allowed to recover for 10 months ($p < 0.01$). However, day-to day variations in thyroxin and methemoglobin in control animals were greater than the differences between the treated and control animals. Erythrocyte counts were increased in males exposed for 3 months and allowed to recover for 19 months ($p < 0.01$). White blood cells were increased in females exposed for 3 or 12 months and allowed to recover up to 22 months ($p < 0.05$). There was no effect of treatment on prothrombin time.

Pathology: There was no effect of treatment on the incidences, distribution or total number of malignancies. One liver angionma was observed in a

control male euthanized at 22 months and one liver adenoma was observed in an exposed female that was moribund after 21.5 months of exposure. The hepatocytes in the adenoma were uniform and had normal appearing nuceli. Focal vacuolization of the cytoplasm of hepatocytes were observed in 22/125 control males, 58/125 exposed males, 18/125 control females and 19/124 exposed females. Liver congestion was observed in 1/125 male controls, 8/125 exposed males, 1/125 control females and 3/124 exposed females. Focal areas of hepatocellular nodules were observed in 2/125 control males, 10/125 exposed males, 1/125 control females and 3/124 exposed females. the cells in the nodular areas were generally hypertrophied, but nuceli were normal. Calcification of the kidney was noted in 76 control animalds and 94 exposed animals.

Source : PCA Services, Inc Durham, NC

Test condition : Animals: Two hundred fifty CRL: COBS CD SD BR rats per sex were used in the study. The initial weights and ages were not listed. Rats were acclimated for an unlisted amount of time. All animals were allowed free access to food and water (except during exposure, when food and water were withheld from both controls and exposed animals). The animals were randomly allocated to an exposure group of 125 animals/sex and a control group of 125 animals/sex.

Generation of vapor: Vapors were generated by bubbling purified nitrogen through the test material in an all-glass vessel maintained in a thermostatted water bath (45 degrees C). The test material in the generator was maintained at a constant level. After each week of operation the remaining test material was discarded and replaced with fresh material. Analyses of the test material remaining after one week showed that the material did not decompose. The effluent from the vapor generator was injected into a section of the chamber containing a large circulating fan that mixed the effluent with air from the inatake air duct. An exhaust blower was operated at a velocity sufficient to provide 15 air changes/hour.

Concentrations of vapors in the exposure chambers were monitored by frequent sampling. Routinely, at least 3 air samples were obtained daily by means of an air-sampling pump operated with a limiting orifice to control flow rate The air from the chamber was withdrawn through two glass impingers aligned in series, filled with ethyl acetate, and immersed in an ice bath. Studies demonstrated that approximately 99% of the test material was trapped in the first impinger. After a suitable sampling period, the contents of the impingers were transferred to a volumetric flask and a known quantity of 1-nitropropane was added as an internal standard. After dilution to volume, an aliqout was injected into a gas chromatograph and compared with standards. The mean concentration of test material was 25 +/- 1 ppm. This was equivalent to 78 mg/m3.

Study conduct: Groups of 125 animals/sex were exposed to 25 ppm, 7 hours/day, 5 days/week for 22 months in an 8 x 8 x 12 foot chamber. The control group was housed in a room having environmental conditions similar to those in the exposure chamber. All animals were observed daily for signs of toxicity. Each animal was weighed weekly.

Ten animals per sex per group were euthanized at the following intervals: one month, 3 months, 9 months and 12 months. Ten animals per group also were euthanized at 6 months, with the exception of exposed males (N= 9). Sixty two and 44 control males and females (respectively) were euthanized at 22 months. Twenty seven and 29 exposed males and females (respectively) were euthanized at 22 months. Additional groups of 6 males and 8 females, and 7 males and 9 females were exposed to test material for 3 or 12 months (respectively) and euthanized at 22 months.

Body and liver, kidney and brain weights were obtained at termination. Blood for hematolgic (hemoglobin, erythrocyte count, white blood cell count, prothrombin time, hematocrit and methemoglobin) and biochemical (serum glutamic-pyruvic transaminase, ornithine carbamyl transferase, thyroxin, and triiodothyronine) analyses was obtained from the aorta at termination.

All animals that died or survived to termination were given complete necropsies. Special attention was given to the liver and the incidence of tissue masses and nodular appearance was noted. Specimens of skin (and subcutis), mammary glands, spleen, lymph node, thymus, muscle, adipose tissue, kidney, urinary bladder, pituitary, adrenal, thyroid, trachea, lung, bronchus, heart, artery, prostate, seminal vesicle, testis, uterus, ovary, salivary gland, esophagus, stomach, small intestine, colon, mesentary, liver, pancreas, eye, ear, brain and any lesions or tumors were obtained from each of the rats and processed for histological examination.

Statistical analysis: Where appropriate, a Student's t test was used to compare treatment group means against controls.

Test substance : Purity of the test material was 95.65 % (by weight). It also contained 3.63% 1-nitropropane, 0.20% nitroethane, 0.51% 2-nitro-2-methylpropane and 0.01% water.

Reliability : (2) valid with restrictions
Only one concentration was tested. Some biochemical and histological analyses that are performed in guideline studies were not conducted.

13.02.2004 (39) (40)

Type : Sub-chronic
Species : rabbit
Sex : male
Strain : New Zealand white
Route of admin. : inhalation
Exposure period : up to 6 months
Frequency of treatm. : 7 hours/day, 5 days/week
Post exposure period :
Doses : 27 or 207 ppm
Control group : yes
NOAEL : = 27 ppm
LOAEL : = 207 ppm
Method : other
Year : 1977
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : The material nitromethane was tested concurrently (at 98 and 745 ppm) in this study. 2-nitropropane also was tested in rats at the same concentrations. Rabbits and rats were exposed in the same chambers. The results for the rat study are described in a different summary.

The number of deaths in each group was not mentioned. Numerical results for each of the parameters were not tabulated.

The authors noted that some of the material may have decomposed during the vaporization process, which was conducted at 75-120 degrees C. Therefore, the possibility exists that a decomposition product contributed to the toxicity.

Since food and water were not withdrawn during exposure, it is possible that some of the material was ingested.

Result : The average (+/- SD) concentrations of test material in the exposure chambers were 27.2 +/- 3.1 ppm and 207 +/- 15 ppm for the nominal

concentrations of 25 and 200 ppm, respectively.

Effects at 207 ppm: The test material had no significant effect on body weight. There also was no effect of treatment on hematology (with the exception of decreases in prothrombin time at 1 and 3 months). Rabbits exposed to 207 ppm had elevated ornithine carbamyl transferase levels at 1 and 3 months. There were no signs of liver or brain edema in any of the rabbits at any of the intervals. There was no effect of treatment on absolute or relative weights of organs. No test-material related gross pathologic changes were noted in any of the tissues in rabbits. Three of the five rabbits exposed to 207 ppm for 1 month had focal areas of moderate to moderately severe hemorrhage and congestion of the alveolar and alveolar duct walls. Interstitial edema and necrosis were present in the hemorrhagic areas. Histopathology of the lungs and other organs was normal in rabbits exposed to test material for 3 or 6 months.

Effects at 27 ppm: The test material had no significant effect on body weight. There was an increase in ornithine carbamyl transferase at 3 months, which appeared to be due to one very high value. At 6 months, ornithine carbamyl transferase concentration was less than control. There were no signs of liver or brain edema in any of the rabbits at any of the intervals. There was no effect of treatment on relative or absolute organ weights, or gross or microscopic pathology of any organ examined.

Source : PCA Services, Inc Durham, NC

Test condition : Animals: Seventy five male, New Zealand rabbits (approximately 2 kg) were acclimated for 14 days. All animals were allowed food and tap water ad libitum. The animals were randomly allocated to 15 groups of 5 animals each.

Generation of vapor: Test material was pumped at a constant flowrate to the vaporization apparatus. Vaporization was accomplished by utlizing a counter-current flow of heated air. The temperatures at the top and bottom of the column were 75 and 120 degrees C, respectively. Air flows were within 18-25 l/min. The concentrated vapor-air mixture was piped to the exposure chamber inlet and diliuted with air flowing at approximately 1000 l/min. The volume of the exposure chambers was 6 cubic meters. Air was supplied by an air conditioning system separate from the general laboratory system. It was controlled for both temperature (21.5 degrees C) and relative humidity (50%. Chamber flowrate was monitored as the pressure drop across a sharp-edged orifice.

Rabbits were housed in the chambers 24 hours/day. They were caged individually in wire mesh stainless steel cages, beneath a dropping pan and rats that were co-exposed. Once per day (just prior to exposure) animals were removed from the chambers and all pans and the chamber interiors were hosed down with hot water and a disinfectant. All cages were exchanged for clean ones once per week.

Each chamber was autosampled approximately every hour for concentration of test material. The samples were analyzed using a calibrated Wilks MIRAN I infrared absorption spectrophotometer (at a wavelength of 3.4 microns). Chamber concentrations were read from the charts twice daily. Nominal concentrations were obtained by noting the volume of compound used during the each day.

Study conduct: Groups of 5 animals were exposed to 25 or 200 ppm (nominal) test material and euthanized at 1 month, 3 months or 6 months. Animals were weighed at unlisted intervals. Blood for hematolgic (hematocrit, hemoglobin, erythrocyte count, prothrombin time and methemoglobin) and biochemical (serum glutamic-pyruvic transaminase, ornithine carbamyl transferase and thyroxin) analyses was obtained from

the marginal ear vein at each termination. All animals that died or survived to termination were given complete necropsies. The liver, kidney, thyroid, lungs plus trachea (both wet and dry) and brain (both wet and dry) were weighed. The lungs, adrenals, bronchi, cerebellum, cerebral hemispheres, eyes, kidneys, liver, spleen, thyroid and trachea were processed and evaluated microscopically.

Statistical analyses: Data were first analyzed using the Kruskal-Wallis one-way analysis of variance with the rejection level set at p = 0.10. Where differences were noted, the Mann-Whitney U test was applied, with the criterion for significance set at p = 0.05.

Test substance : Purity of the test material was 94.45 % (by weight). It also contained 3.07% 1-nitropropane, 1.96% nitroethane, 0.42% 2-nitro-2-methylpropane, 0.03% 2-nitrobutane and < 0.01% water. Other minor impurities were not listed.

Reliability : (2) valid with restrictions
Some biochemical and histological analyses that are performed in guideline studies were not conducted. None of the results are tabulated. Some of the test material may have been ingested. Animals may have been exposed to a decomposition product.

13.02.2004 (35) (36)

Type : Sub-acute
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 7 hours
Frequency of treatm. : 5 consecutive days
Post exposure period : lifetime observation up to 94 weeks post-exposure
Doses : 200 ppm
Control group : yes, concurrent no treatment
Method :
Year : 1986
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : 160 male and 160 female rats were obtained from a commercial supplier. THe animals were housed in stainless steel wire cages, with food and water provided ad libitum except during inhalation exposures. Rats were randomly assigned to groups of 40 per sex per dose.

Chamber atmospheres were generated by bubbling purified nitrogen through liquified 2-NP in a glass vessel maintained in a thermostatted water bath at a temperature of 45C. Sufficient liquid 2-NP to maintain a constant liquid level in the generator was added automatically. Chambers were 75 cubic feet and operated dynamically. The concentration of 2-NP was analyzed by infra-red spectroscopy at least three times per exposure period.

Following the 5 days of exposure, all animals were housed under non-exposure conditions for the remainder of the study.

Animals were observed during the exposure phase and the observation period daily for signs of toxicity. Moribund animals were sacrificed, and those found dead were subjected to histopathologic examination. Animals were weighed weekly during the first 54 weeks of the experiment, and biweekly thereafter. Necropsies were performed on all animals, and the terminal sacrifice was scheduled to begin when any one sex/exposure grou decreased to 25% of the original number. The brain, liver, kidneys, heart, and lungs were weighed. Full pathology was performed on all organs and

tissues.

Data that was expected to be randomly distributed (body and organ weights) was compared for each sec independently using a Students' T-test. Means and standard deviations were also calculated. The incidence of any pathological finding was determined.

Result : There were no overt signs of toxicity during the 5 exposures. Body weights were decreased for treated animals, and the decrease persisted until approximately one month following treatment, at which time there was no significant difference in weight between the treated animals and the controls.

There were no significant findings in organ weights of the treated animals, nor was any pathology noted in any organ except the kidney. There was a slight increase in chronic inflammation and calculi in the kidney, renal pelvis, and bladder. These factors are typical spontaneous factors assocuated with proliferative responses of the transitional epithelium of the urinary tract.

Significantly, the liver, which is the prime target organ of high doses of 2-NP, exhibited NO chemical-related pathology.

Reliability : (2) valid with restrictions
2e (meets generally accepted scientific standards, well-documented, and acceptable for assessment)

12.04.2005 (41)

Type : Sub-acute
Species : rabbit
Sex : male
Strain :
Route of admin. : inhalation
Exposure period : 7 hours
Frequency of treatm. : 3 consecutive days
Post exposure period :
Doses :
Control group : yes, concurrent no treatment
Method :
Year : 1983
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Ten male rabbits, obtained from a commercial supplier, weighed 2-2.5 pounds at the start of treatment. They were randomly assigned to 2 treatment groups. One group was used as controls, and the other group was exposed to 200 ppm of 2-NP vapors in air for 7 hours on 3 consecutive days. Immediately after the last exposure period, the animals were sacrificed and liver samples were removed for assays of soluble and microsomal protein, total glutathione, cytosolic glutathione peroxidase, microsomal superoxide dismutase, and peroxidation of microsomal lipids measuring malondialdehyde.

For each assay, the mean and standard deviations were calculated for control and exposed animals. T-tests were used to compare the two groups for any significant difference.

Result : No significant differences were found between controls and exposed rabbits. In male rats, by comparison,hepatic glutathione was elevated by 73%, and malondialdehyde by a factor of 5.9, after 3 days of 7 hours inhalation of 200 ppm 2-NP.

There were no significant changes in hepatic glutathione levels or microsomal lipid peroxidation found in the rabbit.

Reliability	:	(2) valid with restrictions 2 (meets standard methods with restrictions)

11.04.2005 (42)

Type	:	Sub-acute
Species	:	monkey
Sex	:	male
Strain	:	other: Rhesus
Route of admin.	:	inhalation
Exposure period	:	7 hours
Frequency of treatm.	:	5 consecutive days
Post exposure period	:	Ethane exhalation measurements
Doses	:	0, 200 ppm
Control group	:	yes, concurrent no treatment
Method	:	
Year	:	1984
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method : Two male rhesus monkeys were exposed to 200 ppm of 2-NP in air for 7 hours daily on 5 consecutive days. At the end of the last exposure period, liver biopsies were taken from each monkey, and levels of malondialdehyde, total glutathione, glutathione peroxidase, and protein in the liver tissue were determined. As controls, liver biopsy samples were taken from unexposed male rhesus monkeys from the same holding room as the exposed animals for the same parameters as the treated animals.

Prior to exposure, animals were measured for ethane exhalation by placement for 7 hours daily for 3 consecutive days in order to measure baseline levels. The chamber air was circulated through a closed loop system in which CO2 was removed and replaced with O2, excessive humidity removed by passing the air through a silica gel drying column. Air samples were taken periodically through a sampling port and analyzed by GC. After the biopsies, ethane exhalation from the exposed and control animals was monitored in the same way for 7-hour periods on 2 consecutive days.

Exposure to 2-NP was conducted in a dynamic system. The vapor was monitored by GC during the exposures.

Result : There was no significant difference between control and treated animals for liver biochemical parameters. The values for treated animals was within normal variation for the species.

For ethane exhalation, one monkey exhaled significantly more ethane than the controls and the other treated animal, consistent with elevated baseline levels recorded for the same animal.

Reliability	:	(2) valid with restrictions 2 (meets generally accepted scientific standards, well-documented, and acceptable for assessment)

11.04.2005 (43)

Type	:	Sub-chronic
Species	:	other: cat, rat, rabbit, and guinea pig
Sex	:	no data
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	7 hours
Frequency of treatm.	:	5 days per week for 6 months
Post exposure period	:	
Doses	:	various, up to 40 mg/L
Control group	:	

Method	:	
Year	:	1950
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Two cats, two rats, two rabbits, and two guinea pigs were used. Animals were exposed for 7 hours each day, five days per week for 6 months. Animals were exposed to vapors of 2-NP in a dynamic, whole-body chamber. Concentrations were verified analytically. Animals were weighed 3 times each week. Blood erythrocytes, leucocytes and hemoglobin was determined weekly.
Result	:	Based on mortality, cats appeared to be the most sensitive to 2-NP exposure (mortality at 2.55 mg/L), followed by rats, then rabbits, then the guinea pig (survived all exposures at 2.4 mg/L). In life observations included: dyspnea, cyanosis, prostration, unsteady gait, loss of coordination, twitching, and convulsions regardless of species, and lacrimation, salivation, gastric regurgitation was seen additionally only in cats. There were no pathological alterations noted in rats, rabbits, or guinea pigs. Pathology seen in cats included parenchymal degeneration and focal necrosis of the liver, and slight to moderate degeneration of the heart and kidneys. There were varying degrees of pulmonary edema as well as intra-alveolar hemmorhage and interstitial pneumonitis.
Reliability	:	(2) valid with restrictions 2 (meets generally accepted scientific standards, well-documented, and acceptable for assessment)

12.04.2005 (44)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	S. typhimurium strains TA92, TA98, TA100 and TA1537
Test concentration	:	up to 0.1 ml/plate (98 mg/plate)
Cycotoxic concentr.	:	0.1 ml/plate (without S-9), > 0.1 ml/plate (with S-9)
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1979
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Triphosphopyridine nucleotide is not usually present in S-9. It is unknown if this had an effect on the results.
Result	:	All concentrations tested were positive in strain TA100 with or without either S-9 preparation. All concentrations except 0.0037 ml/plate were positive in strain TA98 with or without either S-9 preparation (with the exception of 0.011 ml/plate with S-9 from Aroclor-treated rats and 0.1 ml/plate undiluted material without activation, which was toxic). Undiluted test material (0.1 ml) was positive in TA1537 with either S-9 preparation and was toxic in the absence of S-9. Undiluted test material (0.1 ml) was positive in TA92 with or without either S-9 preparation and 0.03 ml/plate was positive in TA92 in the presence (but not the absence) of either S-9 preparation. The positive control elicited a positive response at both concentrations in all strains except for TA92 (in the absence or presence of either S-9

preparation) or in TA15347 without S-9.

Source : PCA Services, Inc Durham, NC

Test condition : Bacteria: The tester strains (TA92, TA98, TA100 and TA1537) were stored frozen at -80 degrees C until use. They were thawed and grown for 16 hours at 37 degrees C in a nutrient broth containing 0.5% NaCl.

Test materials: 2-Nitropropane was used as supplied or was diluted with dimethylsulfoxide (DMSO). The positive control for all tests was 1-methyl-2)3a,4,5,6,7,7a-hexahydro-1,2-benizisoxazol-3-yl)-5 nitroimidazole (at 7.5 or 150 mg/plate). Concentrations of test material used in strains TA98 and TA100 were 0.0037, 0.11, 0.03 and 0.1 ml/plate. All controls and test material concentrations (except for 0.1 ml) were tested in TA98 and TA100 on two separate occasions. The materials were tested once in the other strains. The 0.0037 concentration was not tested in strains TA1537 and TA92.

S-9: The studies were performed with two rat liver microsomal activation preparations. One was derived from CD male rats pretreated i.p. with 75 mg/kg/day sodium pentobarbital for 4 days and fasted for 18 hours. The other preparation was derived from male rats injected i.p. with 500 mg/kg Aroclor 1254 five days before liver isolation. The final incubation mixture contained 0.3 ml of the S-9 supernatant, 8 micromolar MgCl2, 22 micromolar KCl, 5 micromolar glucose-6-phosphate, 4 micromolar triphosphopyridine nucleotide (TPN) and 100 micromolar sodium phosphate (pH 7.4). In the negative control mixtures, S-9 and TPN were replaced with a saline buffer solution.

Test material, DMSO or positive control (0.1 ml), 0.5 ml S-9 mix or buffer and 2 ml of 0.7% seed agar containing 0.5 ml of inoculum/ml were added to test tubes. The cell titer of the inoculum was approximately 10E8 organisms/ml. The test tubes were rotated between the palms and the contents poured onto base plates contining either hisitidine-deficient (N=3) or histidine-supplemented (N=1) medium.

All plates were incubated for 72 hours at 37 degrees C. Growth on the supplemented medium was compared with that of control plates for evidence of bacterial inhibition. Revertants on histidine-deficient plates were enumerated, counts were averages, and were compared with controls. The test was considered positive if there was at least a 2-fold increase in revertants that was dose-dependent.

Reliability : (2) valid with restrictions
Purity of the material was not listed.

Flag : Critical study for SIDS endpoint

13.02.2004 (45)

Type : Ames test

System of testing : S. typhimurium strains TA98 and TA100

Test concentration : up to 80 micromoles/plate

Cycotoxic concentr. :

Metabolic activation : with and without

Result : positive

Method : other

Year : 1991

GLP : no data

Test substance : as prescribed by 1.1 - 1.4

Result : The result in strain TA100 in the presence of S-9 was positive at 40 micromoles/plate. All other responses in this strain were negative. In strain TA102, a positive response occurred in cells incubated with 80 micromoles/plate test material in the presence of S-9. All other responses

in this strain were negative (although they increased in a dose-dependent manner).

Source : PCA Services, Inc Durham, NC

Test condition : A preincubation test was performed. The S-9 was isolated from Aroclor-induced Spradue-Dawley rat liver. The S-9 mix contained 0.1 ml S-9, 8 micromolar MgCl2, 33 micromolar KCl, 5 micromolar glucose-6-phosphate, 4 micromolar NADP in 0.1 M sodium phosphate buffer (pH 7.0). The S-9 mix or buffer (0.5 ml) and test material, positive or negative control (0.1 ml) were added to 0.1 ml of the tester strains (overnight cultures of approximately 10E9 bacteria/ml). Each concentration of test material (approximately 10, 20, 40 and 80 micromoles/plate) was assayed in triplicate. The negative control was dimethylsulfoxide and the positive controls were sodium azide and 2-anthramine for TA100 and 1,8-dihydroxyanthraquinone and mitomycin C for TA102 (concentrations were not listed). It was not stated if positive and negative controls also were tested in triplicate.

The test mixtures were incubated for 20 minutes at 37 degrees C in the dark and mixed with 2 ml of top agar in 0.05% NaCl containing 0.05 mM L-histidine and 0.05 mM biotin. The contents were poured onto minimal glucose agar plates. The plates were inubated in the dark at 37 degrees C for 48 hours and revertants were scored.

A positive response was indicated by at least a 3-fold increase in mutants with respect to controls.

Test substance : The test material was obtained from Aldrich Chemical Co. and purified by distillation.

Reliability : (2) valid with restrictions
Results for positive controls were not listed. It is difficult to determine actual test material concentrations since the results were displayed graphically. The criterion for a positive response is usually a 2-fold increase. Individual results were not stated so it is not known if any of the other conditions caused at least a 2-fold increase in revertants.

13.02.2004 (46)

Type : Ames test
System of testing : TA98, TA100, and TA102
Test concentration : 5 umol/plate
Cycotoxic concentr. :
Metabolic activation : without
Result : positive
Method :
Year : 1989
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Mutagenicity of nitroalkanes and the corresponding nitronates was evaluated as described by Fiala et al. (1987) using the preincubation modification of the Salmonella mutagenicity assay (Maron and Ames, 1983). S. typhimurium strains TA98, TA100, and TA102 were used. S9 was not included since Fiala determined that activation is not needed for 2-NP mutagenicity. A response was considered positive when the bacterial count was three times the number of colonies in the solvent controls. The significance of differences between treated groups and control groups was assessed using the Mann-Whitney U-test.

Result : 2-NP was positive in tester strain TA100. The anionic form of 2-NP (propane-2-nitronate) was demonstrated in a prior study to be a much more powerful mutagen that the neutral 2-NP in tester strains TA98 and TA100, with no requirement for S9 activation.

Reliability : (2) valid with restrictions
2 (meets generally accepted scientific standards, well-documented, and

acceptable for assessment)

12.04.2005 (47)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	rat
Sex	:	male
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	up to 48 hours (bone marrow test) and 72 hours (liver micronucleus test)
Doses	:	up to 400 mg/kg
Result	:	ambiguous
Method	:	other
Year	:	1989
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark : The mitotic index could not be determined for cells fixed according to the second method, since mitotic cells were not retained on the slides.

1-Nitropropane also tested negative in the bone marrow and positive in the liver. However, unlike 2-nitropropane, 1-nitropropane produced an increase in the mitotic index of the liver. This study confirms the negative result for both 1-nitropropane and 2-nitropropane in a mouse bone marrow micronucleus test conducted by Kliesch and Adler (Mut. Res 192:181-184, 1987).

The results of Unscheduled DNA Synthesis tests also were discussed in this paper. 1-nitropropane tested negative in this test and 2-nitropropane tested positive.

Result : Bone Marrow Test: Only 5 animals in the 300 mg/kg group survived for 24 hours. Therefore, there were no results for the 48 hour time period for this group. IN the 300 mg/kg group, there was a slight increase in the frequency of micronuclei (2.10 +/- 1.14 micronucleated PCE/1000 PCE in treated vs. 1.08 +/- 1.02 micronucleated PCE/1000 PCE in control). However, the average value for the treated animals was not significantly different from the study control and data from only one animal was outside of the historical control range. The resutls for the other groups were negative. There was no significant effect of treatment on the percentages of PCE. However, in the bone marrow smears of the 300 mg/kg group, an increased incidence of pycnotic erythroblasts was observed.

Based on the results of the test, the authors concluded that the test material did not induce micronuclei in the bone marrow.

Liver Cell Test: Slides from both control and treated animals that were prepared according to the first method had higher frequencies of micronuclei than those prepared by the second method. However, the general outcome of both methods was similar for individual animals and groups. Results of the first method showed a significant increase in the frequency of micronuclei in hepatocytes isolated from rats treated with 25 mg/kg (14.25 +/- 5.46 micronucleated cells/1000 cells in treated vs. 7.34 +/- 1.75 micronucleated cells/1000 cells in control) or 50 mg/kg (32.33 +/- 6.61 micronucleated cells/1000 cells in treated vs. 7.34 +/- 1.75 micronucleated cells/1000 cells in control) test material. The value at 75 mg/kg (24.86 +/- 10.13) also was higher than control, but not significantly. The mitotic index of cells from rats exposed to 25 mg/kg (8.83 +/- 1.43) and 75 mg/kg (9.29 +/- 2.20) was significantly lower than control (14.92 +/- 1.39).

For the second method, only the results at 50 mg/kg (21.83 +/- 4.58 micronucleated cells/1000 cells) were significantly different from control (5.03 +/- 0.90 micronucleated cells/1000 cells). At 25 and 75 mg/kg, the numbers of micronucleated cells were increased in 2/6 and 4/7 animals, respectively. The average values in these group were elevated (8.08 +/- 2.76 and 14.53 +/- 4.54 micronucleated cells/1000 cells, respectively), but were not significantly different from the control value listed above.

Based on the results of the test, the authors concluded that the test material induced micronuclei in hepatocytes.

Source : PCA Services, Inc Durham, NC

Test condition : Animals: Male Sprague-Dawley rats aged 8-12 weeks were used. They were allowed free access to food and water.

Bone Marrow tests: Groups of 5-6 animals received 50 or 100 mg/kg test material in a volume of 10 ml/kg body weight by gavage. One group of 11 animals was given 300 mg/kg test material. Doses > 100 mg/kg were given as liquid/liquid suspensions due to insolubility. Two negative control groups of 6 animals/each and one positive control group of 4 animals received water or 8 mg/kg cyclophosphamide, respectively. Six animals/group were euthanized at 24 hours, and the other six/group were euthanized at 48 hours (with the exception of the positive control group, which was euthanized at 24 hours). There was no 300 mg/kg group for the 48 hour test point.

Bone marrow smears were prepared according to procedures listed in Pascoe and Gatehouse, Mut. Res. 164:237-243, 1986, and were stained with hematoxylin-eosin. Slides were coded prior to analysis. Two thousand polychromatic erythrocytes (PCE) per slide were analyzed for the presence of micronuclei, and 500 erythrocytes per slide were scored to determine the proportion of PCE among all erythrocytes. Data were analyzed according to methods published by Amphlett and Delow (Mut. Res. 128:161-164, 1984).

Liver micronucleus test: A liver micronucleus test was performed on an additional group of 8 control animals and groups of 6-7 animals treated by gavage with 25, 50 or 75 mg/kg test material. The test was performed according to the method developed by Braithwaite and Ashby (Mut. Res. 203:23-32, 1988). Three days after dosing, the animals received a single oral dose of 1000 mg/kg 4-acetylaminofluorene. Two days later, hepatocytes were isolated according to the procedure of Ashby et al (Mut. Res.156:1-18, 1985), with the exception that the perfusion buffers were not gassed with air and did not contain antibiotics.

Two methods of slide preparation were used. For the first method, hepatocytes were fixed directly with methanol/acetic acid (3:1) and spun in a centrifuge (50 g) for 2 minutes. The supernatant was removed and the fixation procedure was repeated twice. Slides of the suspension were prepared, checked under phase contrast (10x magnification) for appropriate cell density and air-dried.

For the second method, hepatocytes were allowed to attach for 3-4 hours on coverslips, rinsed with medium, and fixed in 85:10:5 methanol/acetic acid/formaldehyde (37%) for 30 minutes. After this, the coverslips were rinsed with distilled water, allowed to dry and mounted on microscope slides. All slides prepared by this method were placed in 5 M hydrochloric acid for an hour, rinsed in distilled water, and placed in Schiff's reagent for 20 minutes, followed by distilled water for 10 minutes. The cytoplasm was stained with 0.5% light green for 2 minutes, after which the slides were air dried and coded.

For each slide preparation method, a minimum of 2000 hepatocytes per animals were analyzed under 1000x magnification for the presence of micronuclei according to the scoring criteria of Braithwaite and Ashby (Mut. Res. 203:23-32, 1988). For the slides prepared by the first method, the number of mitoses was determined in at least 2000 hepatocytes per animal. Data were analyzed for normal distribution and compared using either the Student's t-test or analysis of variance. The critical level of significance was $p < 0.05$.

Test substance : The test material was used as supplied by Aldrich. Considering the source, it is likely that the material was of high purity.

Reliability : (1) valid without restriction
The study is comparable to a guideline test.

Flag : Critical study for SIDS endpoint

12.04.2005 (48)

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain :
Route of admin. : i.p.
Exposure period :
Doses : 0.1mL/10g body weight
Result : negative
Method :
Year : 1987
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Groups of 5 male and 5 female mice, aged 12-14 weeks, were injected with 0.1 mL/10g body weight. Animals were randomly allotted to treatment groups, and paired with animals that received the solvent only (physiological saline). Bone marrow preparations were carried out under standard methods, and the micronucleus frequency was determined by analyzing 2000 polychromatic erythrocytes (PCE) per animal from coded slides. The numbers of PCE were counted in the microscopic fields that showed 2000 normochromatic erythrocytes (NCE) per animal to determine the NCE/PCE ratio as a measure of cytotoxicity.

Result : The highest frequency of micronucleated polychromatic erythrocytes was 0.26%, not statistically elevated from the control group. Experiments with 2NP or 1NP did not reveal any clastogenic activity of the compounds. No dose- or time-dependent increase in the number of PCE were found. There was no increase in micronucleus rates at 300 mg/kg at either 24 or 72 hours. A single positive finding at 200 mg/kg was not reproducible or dose-dependent.

Reliability : (2) valid with restrictions
2 (meets generally accepted scientific standards, well-documented, and acceptable for assessment)

12.04.2005 (49)

5.7 CARCINOGENICITY

Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 6 months
Frequency of treatm. : 7 hours/day, 5 days/week
Post exposure period :

Doses	:	27 or 207 ppm
Result	:	positive
Control group	:	yes
Method	:	other
Year	:	1977
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Remark : This study is described in detail in section 5.4. Only the methods and results pertaining to histopathology are presented in this summary.

The high dose for the study was originally 400 ppm (instead of 200 ppm). However, since excessive mortality occurred within 3 days, the exposure was stopped. New groups of rats with average weights of 96 g were then exposed to 200 ppm (nominal). These animals weighed less than controls or rats exposed to 27 ppm (avg. weight 171 g). Therefore, results for rats exposed to 207 ppm were compared to those of controls that had significantly higher weights. A new control group comprised of rats with weights approximating those of rats exposed to 207 ppm should have been added when animals were exposed to 207 ppm.

The authors noted that some of the material may have decomposed during the vaporization process, which was conducted at 75-120 degrees C. Therefore, the possibility exists that a decomposition product contributed to the toxicity.

Since food and water were not withdrawn during exposure, it is possible that some of the material was ingested.

Result : The average (+/- SD) concentrations of test material in the exposure chambers were 27.2 +/ - 3.1 ppm and 207 +/- 15 ppm for the nominal concentrations of 25 and 200 ppm, respectively.

Effects at 207 ppm: There was no effect of treatment on body weight. At 1, 3 and 6 months, rats exposed to 207 ppm had an increased incidence dark hemorrhagic foci in the lungs. The livers of rats exposed to 207 ppm for 3 months had areas of necrosis and surface lesions and were paler in color than controls. After 6 months of exposure to 207 ppm, the livers were enlarged and pale with numerous masses and lesions.

No exposure-related microscopic alterations were seen in any of the tissues of rats exposed for 2 or 10 days, or 1 month. In all 9 rats euthanized after exposure to 207 ppm test material for 3 months, numerous focal areas of hepatocellular hypertrophy were noted. The hepatocytes in these foci were more eosinophilic than the surrounding cells and usually contained large, vesiculated nuclei. In 4 of the 9 rats, basophilic foci containing hyperplastic, small hepatocytes with hyperchromatic nuclei were observed. Occasionally, mitotic figures were present.

Multiple hepatocellular carcinomas and numerous neoplastic nodules were present in the livers of all 10 rats exposed to 207 ppm test material for 6 months. In many cases, the normal hepatic parenchyma was destroyed. The neoplasms were composed of anaplastic hepatocytes, sometimes forming broad sheets or trabeculae several cells thick. Blood-filled cysts were occasionally seen in the neoplasm. Mitotic figures were commonly observed. The carcinomas appeared to be rapidly growing. However, no metastatic hepatocellular carcinomas were seen in any of the other tissues examined.

Effects at 27 ppm : There was no effect of treatment on body weight. No exposure-related macroscopic or microscopic changes were observed in

any organ that was examined.

Source : PCA Services, Inc Durham, NC

Test condition : Animals: Two hundred fifty male, Sprague-Dawley rats (100 g) were acclimated for 14 days. All animals were allowed food and tap water ad libitum. The animals were randomly allocated to 25 groups of 10 animals each.

Generation of vapor: Test material was pumped at a constant flowrate to the vaporization apparatus. Vaporization was accomplished by utlizing a counter-current flow of heated air. The temperatures at the top and bottom of the column were 75 and 120 degrees C, respectively. Air flows were within 18-25 l/min. The concentrated vapor-air mixture was piped to the exposure chamber inlet and diliuted with air flowing at approximately 1000 l/min. The volume of the exposure chambers was 6 cubic meters. Air was supplied by an air conditioning system separate from the general laboratory system. It was controlled for both temperature (21.5 degrees C) and relative humidity (50%. Chamber flowrate was monitored as the pressure drop across a sharp-edged orifice.

Rats were housed in the chambers 24 hours/day. They were caged (10/cage) in wire mesh stainless steel cages, with a dropping pan beneath. Once per day (just prior to exposure) animals were removed from the chambers and all pans and the chamber interiors were hosed down with hot water and a disinfectant. All cages were exchanged for clean ones once per week.

Each chamber was autosampled approximately every hour for concentration of test material. The samples were analyzed using a calibrated Wilks MIRAN I infrared absorption spectrophotometer (at a wavelength of 3.4 microns). Chamber concentrations were read from the charts twice daily. Nominal concentrations were obtained by noting the volume of compound used during the each day.

Study conduct: Groups of 10 animals were exposed to 25 or 200 ppm (nominal) test material and euthanized at 2 days, 10 days, 1 month, 3 months or 6 months. Animals were weighed at unlisted intervals. All animals that died or survived to termination were given complete necropsies. The liver, kidney, thyroid, lungs plus trachea (both wet and dry) and brain (both wet and dry) were weighed. The lungs, adrenals, bronchi, cerebellum, cerebral hemispheres, eyes, kidneys, liver, spleen, thyroid and trachea were processed and evaluated microscopically.

Statistical analyses: Data were first evaluated for homogeneity using Bartlett's test, with the rejection level set at $p = 0.01$. A one-way analysis of variance was then conducted (with the critical value set at $p = 0.10$). Data that were significantly different were then analyzed with the Student's t-test to determine which means were significantly different from control. The critical value for these analyses was $P = 0.05$.

Test substance : Purity of the test material was 94.45 % (by weight). It also contained 3.07% 1-nitropropane, 1.96% nitroethane, 0.42% 2-nitro-2-methylpropane, 0.03% 2-nitrobutane and < 0.01% water. Other minor impurities were not listed.

Reliability : (2) valid with restrictions
Some biochemical analyses that are performed in guideline studies were not conducted. Some of the test material may have been ingested. Animals may have been exposed to a decomposition product. Weights of high dose animals were significantly less than controls.

11.02.2004 (35) (36)

Species : rat

Sex : male/female

Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	12 or 18 months
Frequency of treatm.	:	7 hours/day, 5 days/week
Post exposure period	:	up to 9 months exposure for some rats followed by 9 months of recovery
Doses	:	100 ppm
Result	:	positive
Control group	:	yes
Method	:	other
Year	:	1983
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark : This study is described in detail in section 5.4. Only the methods and results pertaining to histopathology are presented in this summary.

It is not known whether the incidences of tumors are for main study and recovery animals or just for main study animals. Appendices that listed incidences of lesions were not included with the report.

Result : Main test animals: Males exposed for up to 12 months and females exposed for up to 18 months had similar body weights as controls. Males exposed for 18 months had lower body weights than controls. Hepatic lesions were observed in males exposed for 9, 12, or 18 months, with the frequency increasing with length of exposure (6/16, 5/10 and 22/23, respectively). Hepatic lesions were also found in 11/16 males found dead or moribund. Hepatic lesions were also noted in 1/20 females exposed for 9 months and 2/30 exposed for 18 months. None of the 5 females that were found dead or moribund had liver lesions.

Recovery animals: Body weights of males exposed for 3 months and allowed to recover for 15 months and of females in all recovery groups were similar to controls. Males exposed for 6 or 9 months and allowed to recover for 12 or 9 months (respectively) had reduced body weights compared to controls. Hepatic lesions were observed in males exposed for 3, 6, or 9 months that were allowed to recover in similar frequency (6/10, 7/10 and 7/10, respectively). Lesions were also found in livers of 2/10 females in the 9 month treatment/9 month recovery group.

Pathology report:
Neoplasms: The total number of tumors in the unexposed group (43) exceeded the total number of tumors in the exposed group (25). The total number of animals with tumors in the control group (38) also was greater than the exposed group (23). The types of tumors observed in exposed and control females were similar. The most common benign and malignant tumors in control and exposed females were pituitary adenoma and mammary gland adenocarcinoma, respectively. The types of tumors observed in exposed and control males were different. The most common benign and malignant tumors in control males were pituitary adenoma (N= 6) and fibrosarcoma of the skin and sucutis (N = 1). In exposed males the most common benign tumor also was pituitary adenoma (N= 1). However, the most common malignant tumor in exposed males was hepatocellular carcinoma (N=7).

Non-neoplastic pathology: There was an increase in renal calcification in exposed males and females compared to controls. Focal necrosis, vacuolar degeneration and nodular hyperplasia were increased in exposed males and females.

Source : PCA Services, Inc Durham, NC

Test condition : Animals: Two hundred fifty CRL: COBS CD SD BR rats per sex were used in the study. The initial weights and ages were not listed. Rats were acclimated for an unlisted amount of time. All animals were allowed free

access to food and water (except during exposure, when food and water were withheld from both controls and exposed animals). The animals were randomly allocated to an exposure group of 125 animals/sex and a control group of 125 animals/sex.

Generation of vapor: Vapors were generated by bubbling purified nitrogen through the test material in an all-glass vessel maintained in a thermostatted water bath (45 degrees C). The test material in the generator was maintained at a constant level. After each week of operation the remaining test material was discarded and replaced with fresh material. Analyses of the test material remaining after one week showed that the material did not decompose. The effluent from the vapor generator was injected into a section of the chamber containing a large circulating fan that mixed the effluent with air from the inatake air duct. An exhaust blower was operated at a velocity sufficient to provide 15 air changes/hour.

Concentrations of vapors in the exposure chambers were monitored by frequent sampling. Routinely, at least 3 air samples were obtained daily by means of an air-sampling pump operated with a limiting orifice to control flow rate The air from the chamber was withdrawn through two glass impingers aligned in series, filled with ethyl acetate, and immersed in an ice bath. Studies demonstrated that approximately 99% of the test material was trapped in the first impinger. After a suitable sampling period, the contents of the impingers were transferred to a volumetric flask and a known quantity of 1-nitropropane was added as an internal standard. After dilution to volume, an aliqout was injected into a gas chromatograph and compared with standards. The mean concentration of test material was 100 +/- 3ppm. This was equivalent to 312 mg/m3.

Study conduct: Groups of 125 animals/sex were exposed to 100 ppm, 7 hours/day, 5 days/week in 8 x 8 x 12 foot chambers. The control group was housed in a room having environmental conditions similar to those in the exposure chamber. All animals were observed daily for signs of toxicity.

Ten animals per sex per group were euthanized at the following intervals: one month, 3 months, 6 months, 9 months and 12 months. Sixty two and 67 control males and females (respectively) were euthanized at 18 months. Twenty three and 30 exposed males and females (respectively) were euthanized at 18 months. Additional groups of 7 males and 10 females, 8 males and 10 females and 7 males and 8 females were exposed to test material for 3, 6 of 9 months (respectively) and euthanized at 18 months.

All animals that died or survived to termination were given complete necropsies. Special attention was given to the liver and the incidence of tissue masses and nodular appearance was noted. Specimens of lung, liver, kidney, lymph node and any unusual lesions were obtained from each of the rats and processed for histological examination.

Test substance : Purity of the test material was 95.65 % (by weight). It also contained 3.63% 1-nitropropane, 0.20% nitroethane, 0.51% 2-nitro-2-methylpropane and 0.01% water.

Conclusion : There is a small increase in the incidence of hepatocellular carcinoma compared to controls.

Reliability : (2) valid with restrictions
Data were not analyzed statistically. Only one concentration was tested.

11.02.2004 (37) (38)

Species : rat
Sex : male/female
Strain : Sprague-Dawley

Route of admin.	:	inhalation
Exposure period	:	22 months
Frequency of treatm.	:	7 hours/day, 5 days/week
Post exposure period	:	
Doses	:	25 ppm
Result	:	negative
Control group	:	yes
Method	:	other
Year	:	1980
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark : This study is described in detail in section 5.4. Only the methods and results pertaining to histopathology are presented in this summary.

Result : There was no effect of treatment on the incidences, distribution or total number of malignancies. One liver angioma was observed in a control male euthanized at 22 months and one liver adenoma was observed in an exposed female that was moribund after 21.5 months of exposure. The hepatocytes in the adenoma were uniform and had normal appearing nuceli. Focal vacuolization of the cytoplasm of hepatocytes were observed in 22/125 control males, 58/125 exposed males, 18/125 control females and 19/124 exposed females. Liver congestion was observed in 1/125 male controls, 8/125 exposed males, 1/125 control females and 3/124 exposed females. Focal areas of hepatocellular nodules were observed in 2/125 control males, 10/125 exposed males, 1/125 control females and 3/124 exposed females. The cells in the nodular areas were generally hypertrophied, but nuceli were normal. Calcification of the kidney was noted in 76 control animalds and 94 exposed animals.

Source : PCA Services, Inc Durham, NC

Test condition : Animals: Two hundred fifty CRL: COBS CD SD BR rats per sex were used in the study. The initial weights and ages were not listed. Rats were acclimated for an unlisted amount of time. All animals were allowed free access to food and water (except during exposure, when food and water were withheld from both controls and exposed animals). The animals were randomly allocated to an exposure group of 125 animals/sex and a control group of 125 animals/sex.

Generation of vapor: Vapors were generated by bubbling purified nitrogen through the test material in an all-glass vessel maintained in a thermostatted water bath (45 degrees C). The test material in the generator was maintained at a constant level. After each week of operation the remaining test material was discarded and replaced with fresh material. Analyses of the test material remaining after one week showed that the material did not decompose. The effluent from the vapor generator was injected into a section of the chamber containing a large circulating fan that mixed the effluent with air from the inatake air duct. An exhaust blower was operated at a velocity sufficient to provide 15 air changes/hour.

Concentrations of vapors in the exposure chambers were monitored by frequent sampling. Routinely, at least 3 air samples were obtained daily by means of an air-sampling pump operated with a limiting orifice to control flow rate The air from the chamber was withdrawn through two glass impingers aligned in series, filled with ethyl acetate, and immersed in an ice bath. Studies demonstrated that approximately 99% of the test material was trapped in the first impinger. After a suitable sampling period, the contents of the impingers were transferred to a volumetric flask and a known quantity of 1-nitropropane was added as an internal standard. After dilution to volume, an aliqout was injected into a gas chromatograph and compared with standards. The mean concentration of test material was 25 +/- 1 ppm. This was equivalent to 78 mg/m3.

Study conduct: Groups of 125 animals/sex were exposed to 25 ppm, 7 hours/day, 5 days/week for 22 months in an 8 x 8 x 12 foot chamber. The control group was housed in a room having environmental conditions similar to those in the exposure chamber. All animals were observed daily for signs of toxicity. Each animal was weighed weekly.

Ten animals per sex per group were euthanized at the following intervals: one month, 3 months, 9 months and 12 months. Ten animals per group also were euthanized at 6 months, with the exception of exposed males (N= 9). Sixty two and 44 control males and females (respectively) were euthanized at 22 months. Twenty seven and 29 exposed males and females (respectively) were euthanized at 22 months. Additional groups of 6 males and 8 females, and 7 males and 9 females were exposed to test material for 3 or 12 months (respectively) and euthanized at 22 months.

All animals that died or survived to termination were given complete necropsies. Special attention was given to the liver and the incidence of tissue masses and nodular appearance was noted. Specimens of skin (and subcutis), mammary glands, spleen, lymph node, thymus, muscle, adipose tissue, kidney, uirnary bladder, pituitary, adrenal, thyroid, trachea, lung, bronchus, heart, artery, prostate, seminal vesicle, testis, uterus, ovary, salivary gland, esophagus, stomach, small intestine, colon, mesentary, liver, pancreas, eye, ear, brain and any lesions or tumors were obtained from each of the rats and processed for histological examination.

Statistical analysis: Where appropriate, a Student's t test was used to compare treatment group means against controls.

Test substance : Purity of the test material was 95.65 % (by weight). It also contained 3.63% 1-nitropropane, 0.20% nitroethane, 0.51% 2-nitro-2-methylpropane and 0.01% water.

Reliability : (2) valid with restrictions
11.02.2004 (39) (40)

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	i.p.
Exposure period	:	days 1-15 of gestation
Frequency of treatm.	:	daily
Duration of test	:	to day 21 of gestation
Doses	:	170 mg/kg
Control group	:	yes
NOAEL maternal tox.	:	= 170 mg/kg bw
NOAEL teratogen.	:	= 170 mg/kg bw
NOAEL Fetotoxicity	:	< 170 mg/kg bw
Result	:	positive for fetal toxicity but was not teratogenic
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark : It was stated that the dose administered to females was one that did not cause mortality, no marked signs of toxicity and less than a 10% reduction

in body weight gain over the course of 15 daily ip injections in previously tested non-pregnant rats.

It is unknown what is meant by "delayed heart development". Specific alterations in the hearts of fetuses were not mentioned.

Result : The development of the heart was delayed by 1-2 days. There was no evidence of teratogenicity and no treatment-related histopathological changes in maternal tissues. There was no effect of treatment on maternal organ weights.

Source : PCA Services, Inc Durham, NC

Test condition : Young adult female Sprague-Dawley rats (250-300 g) were caged with breeder males of the same strain. Females were examined daily for the presence of sperm in a vaginal lavage. The day sperm was detected was designated as day 1 of gestation. Inseminated females were randomly allocated to a control or treatment group (N = 10-15/group). Groups were injected ip with 170 mg/kg test material or corn oil daily from days 1-15 of gestation.

On day 21 of gestation, the females were euthanized and the uterine contents were examined. The internal organs were examined grossly and the brain, heart, liver, lungs, spleen, kidneys, adrenals and ovaries were weighed and preserved in 10% formalin for histopathological examination.

The individual fetuses were weighed, measured for crown-rump length, sexed and examined for external malformations. One half to two thirds of each litter was preserved in Bouin's solution for internal examination by the Wilson method of free-hand razor-blade sectioning, and the rest of the fetuses were fixed in ethanol for clearing and skeletal staining with alizarin red.

Statistical methods were not listed. The level for significance was listed as $p < 0.05$.

Reliability : (4) not assignable
The study was performed with a route of exposure that is not relevant for humans. Evidence for the conclusion of "delayed heart development" was not presented.

13.02.2004 (50)

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : i.p.
Exposure period : days 1-15 of gestation
Frequency of treatm. : daily
Duration of test : one day prior to parturition
Doses : 170 mg/kg
Control group : yes
Method : other
Year : 1979
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Three other materials were tested in this study. Data for 2-nitropropane were reproduced verbatim. No other information about 2-nitropropane was listed.

Result : Retarded heart development (1-2 days) was observed in 9 out of 10 litters from mothers treated with 2-nitropropane ($p < 0.001$). Thirty to 86 percent of the pups examined within a litter were affected.

Source : PCA Services, Inc Durham, NC

Test condition : Adult female Sprague-Dawley rats were injected with 170 mg/kg bw 2-nitropropane (2-NP) or 1 ml/kg bw corn oil (C) on days 1-15 of gestation.

Litters were collected one day prior to parturition and examined by the techniques of Wilson and Dawson.

Reliability : (4) not assignable
Information was obtained from an abstract. There is no information about maternal toxicity. Numbers of animals tested were not listed. The study was performed with a route of exposure that is not relevant for humans. Evidence for the conclusion of "delayed heart development" was not presented.

13.02.2004 (51)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type	:	other: examination of reproductive organs from chronic toxicity study
In vitro/in vivo	:	In vivo
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	22 months
Frequency of treatm.	:	7 hours/day, 5 days/week
Duration of test	:	22 months
Doses	:	25 ppm
Control group	:	yes
Result	:	negative
Method	:	other
Year	:	1980
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark : This study is described in greater detail in Section 5.4. Only the test conditions and results pertinent to reproductive organs are listed in this summary.

Result : There was no evidence of any lesion or onset of any disease in any organ examined that could be attributed to test material exposure. Therefore, 25 ppm is a NOAEL for reproductive organ toxicity.

Source : PCA Services, Inc Durham, NC

Test condition : nimals: Two hundred fifty CRL: COBS CD SD BR rats per sex were used in the study. The initial weights and ages were not listed. Rats were acclimated for an unlisted amount of time. All animals were allowed free access to food and water (except during exposure, when food and water were withheld from both controls and exposed animals). The animals were randomly allocated to an exposure group of 125 animals/sex and a control group of 125 animals/sex.

Generation of vapor: Vapors were generated by bubbling purified nitrogen through the test material in an all-glass vessel maintained in a thermostatted water bath (45 degrees C). The test material in the generator was maintained at a constant level. After each week of operation the remaining test material was discarded and replaced with fresh material. Analyses of the test material remaining after one week showed that the material did not decompose. The effluent from the vapor generator was injected into a section of the chamber containing a large circulating fan that mixed the effluent with air from the inatake air duct. An exhaust blower was operated at a velocity sufficient to provide 15 air changes/hour.

Concentrations of vapors in the exposure chambers were monitored by frequent sampling. Routinely, at least 3 air samples were obtained daily by means of an air-sampling pump operated with a limiting orifice to control

flow rate The air from the chamber was withdrawn through two glass impingers aligned in series, filled with ethyl acetate, and immersed in an ice bath. Studies demonstrated that approximately 99% of the test material was trapped in the first impinger. After a suitable sampling period, the contents of the impingers were transferred to a volumetric flask and a known quantity of 1-nitropropane was added as an internal standard. After dilution to volume, an aliqout was injected into a gas chromatograph and compared with standards. The mean concentration of test material was 25 +/- 1 ppm. This was equivalent to 78 mg/m3.

Study conduct: Groups of 125 animals/sex were exposed to 25 ppm, 7 hours/day, 5 days/week for 22 months in an 8 x 8 x 12 foot chamber. The control group was housed in a room having environmental conditions similar to those in the exposure chamber. All animals were observed daily for signs of toxicity. Each animal was weighed weekly.

Ten animals per sex per group were euthanized at the following intervals: one month, 3 months, 9 months and 12 months. Ten animals per group also were euthanized at 6 months, with the exception of exposed males (N= 9). Sixty two and 44 control males and females (respectively) were euthanized at 22 months. Twenty seven and 29 exposed males and females (respectively) were euthanized at 22 months. Additional groups of 6 males and 8 females, and 7 males and 9 females were exposed to test material for 3 or 12 months (respectively) and euthanized at 22 months.

Body weights were obtained at termination. All animals that died or survived to termination were given complete necropsies. Specimens of prostate, seminal vesicle, testis, uterus, ovary and any lesions or tumors were obtained from each of the rats and processed for histological examination.

Statistical analysis: Where appropriate, a Student's t test was used to compare treatment group means against controls.

Test substance : Purity of the test material was 95.65 % (by weight). It also contained 3.63% 1-nitropropane, 0.20% nitroethane, 0.51% 2-nitro-2-methylpropane and 0.01% water.

Reliability : (2) valid with restrictions
Animals were not mated. Incidences of findings in controls and treated animals were not tabulated (and therefore could not be examined). The result listed under the "result" heading was written in the text.

13.02.2004 (39) (40)

Type : other: dominant lethal test
In vitro/in vivo : In vivo
Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 5 days
Frequency of treatm. : 7 hours/day
Duration of test : to 17 days after mating
Doses : 25 and 200 ppm
Control group : yes
Result : negative
Method : other
Year : 1981
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : This study was one of four different genetic toxicity tests performed in the investigation.

Result : Test material concentrations: The atmosphere was homogeneous within the chamber. For the 25 and 200 ppm concentrations , the maxiumum devations were -4% and +2%, respecetively. During the study, there were only a few occasions where the concentration of test material deviated from the target concentration by more than 10%.

Results at 200 ppm : There were no clinical signs of toxicity on the first 2 days of exposure. Loss of muscle tone was observed on day 3. Body weights of exposed animals were less than control. As assessed by either corpora lutea graviditatis or the numbers of females with implantations, the pregnancy frequency ranged from 75-95% in exposed animals vs. 80-100% in control. The numbers of corpora lutea or total implantations per pregnancy were not reduced in exposed animals. Small reductions in the frequencies of live implantations and live implantations and late deaths (both were 11.7 +/- 0.58 in exposed vs. 13.4 +/- 0.58 in control) were observed in females from the second mating group only. However, the value for exposed animals was within the range of controls for the whole study (11.6 - 13.4). There was no effect of exposure on the frequency of early death (as assessed by either method) or on the numbers of animals with one or more or two or more early deaths.

Results at 25 ppm: No clinical signs of toxcity were observed. As assessed by either corpora lutea graviditatis or the numbers of females with implantations, the pregnancy frequency ranged from 90-100% in exposed animals vs. 80-100% in control. The numbers of corpora lutea or total implantations per pregnancy were not reduced in exposed animals. There was no effect on the frequencies of live implantations and live implantations and late deaths. There was no effect of exposure on the frequency of early death (as assessed by either method) or on the numbers of animals with one or more or two or more early deaths.

Positive control group: Body weights of exposed animals were less than control. As assessed by either corpora lutea graviditatis, the pregnancy frequency ranged from 50-100% in exposed animals vs. 80-100% in control. As assessed by the numbers of females with implantations, the pregnancy frequency ranged from 10-100% in exposed animals vs. 80-100% in control. The numbers of corpora lutea and total implantations were reduced in rats in the first 5 and 4mating groups, respectively. Large reductions in the frequencies of live implantations and live implantations and late deaths (both were 11.7 +/- 0.58 in exposed vs. 13.4 +/- 0.58 in control) were observed in females in the first four mating groups. The frequency of early death increased in females in the first and fourth mating groups (as assessed by the Poisson transformation) and in the first 4 mating groups (as assessed by binomial transformation).

Source : PCA Services, Inc Durham, NC

Test condition : Animals: Two hundred twenty male CD rats (10-11 weeks old) were acclimated for at least 7 days before treatment. all animals were examined on arrival for signs of ill health. Twenty sentinel rats had no evidence of infection. Animals were individually housed (except during mating) and were allowed free access to food and water (except during exposure, when they were withheld). Four groups of 10 randomly allocated animals were used in the study.

Exposure conditions: Exposures were carried out in 1.5 m3 chambers constructed of stainless steel and glass. The breathing zone was ventilated at a rate of 12 air changes per hour. An additional chamber of 0.84 m3 capcacity was used for the air control group. The breathing zone of this chamber was ventilated at a rate of 6 air changes per hour. Compressed, filtered, conditioned and oil-free air was supplied through compressors fitted with automatic pressure control switches. Test atmospheres were exhausted from the exposure chambers with a Gast

extract pump. The chambers were maintained under slight negative pressure to minimize leakage. Animal positions were rotated on a daily basis.

The test atmosphere was generated by bubbling dry, oxygen-free nitrogen through a liquid reservoir of 2-nitropropane immersed in a water bath maintained at 30 degrees C. Test material was added to the reservoir daily. The vapor mixture was ducted through stainless steel piping to a glass mising vessel and diluted with compressed air. The resulting mixture was piped to the top of the exposure chamber. Concentrations of test material were maintained by regulating the flow of nitrogen and air into the mixing vessels using adjustable flowmeters.

Concentrations of test material in the atmospheres were analyzed by infrared spectroscopy (11.8 microns wavelength). Samples collected from the breathing zone were continuously pumped (5 l/min) through stainless steel sample lines to the gas cell of the analyzer. The analyzer was calibrated daily. The concentration was measured and relayed to a chart recorder.

Test conduct: Groups of animals were exposed to air (control), or 25 or 200 ppm test material 7 hours/day, for 5 days. Animals were observed for clinical signs after exposure. A positive control group was treated with 100 mg/kg ethylmethanesulphonate by gavage for 5 consecutive days. Positive control animals were not allowed access to food or water while the other animals were being exposed.

After treatment, two virgin females were introduced to each of the 40 cages containing single, exposed male rats. Males were removed from the females on day 12 (7 days afer the last exposure). On day 22 (17 days after the last exposure), females were euthanized and examined for pregnancy and dominant lethal effects. The mating procedure was repeated and pregnancy status was examined on each of the next 9 consecutive weeks.

Ovaries were examined for corpora lutea gravidatatis and uteri were examined for live implanatations and early and late deaths. Live implantations were those fetuses that had a clearly functioning vasculature at time of maternal death. A fetus that showed evidence of organogenesis but was bloodless was classified as a late death. An early death was diagnosed as a point of uterine reaction to an implanting blastula, charaterized by a small, raised, discrete spot along the line of implantation consisting mostly of deoxygenated and clotted blood. Pregnancy was defined as females with corpora lutea gravidatatis and females with implantations.

Statistical analyses: Data for the negative control, and low and high doses of test material were analyzed together. Data for the positive control were analyzed separately. The proportion of females with one or more, or 2 or more early deaths and the fertility index were calculated. These data were analyzed using a chi-square test. Early deaths were analyzed using Freeman-Tukey Poisson or Freeman-Tukey Binomial Transformations. The critical value for significance was $p < 0.05$ (with the exception of the Poisson Tranformation, in which it was $p < 0.01$).

Test substance : The test material had a stated purity of 94%. It was used as received from AMC Chemical Group Incorporated.

Conclusion : The authors concluded that 2-nitropropane does not cause dominant lethal mutations in rats.

Reliability : (2) valid with restrictions
The study is comparable to a guideline test. However, the utility for assessing reproductive toxicity is limited due to the fact that males were

only exposed for 5 days before mating and females were not exposed at all.

12.02.2004 (52)

Type	:	other: sperm abnormality test
In vitro/in vivo	:	In vivo
Species	:	mouse
Sex	:	male
Strain	:	B6C3F1
Route of admin.	:	inhalation
Exposure period	:	5 days
Frequency of treatm.	:	7 hours/day
Duration of test	:	5 weeks after last exposure
Doses	:	25 and 200 ppm
Control group	:	yes
Result	:	negative
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Result : The atmosphere was homogeneous within the chamber. For the 25 and 200 ppm concentrations, the maxiumum devations were -4% and +2%, respecetively. During the study, there were only a few occasions where the concentration of test material deviated from the target concentration by more than 10%.

There was no significant effect of treatment on body weight. Mice were slightly subdued after day 2 of exposure (concentration was not listed), but it was not clear if this was related to exposure since it persisted for 3 weeks.

There were no increases in the frequency of abnormal sperm in any of the categories examined in exposed animals. EMS also did not have a significant effect on sperm abnormalities.

Source : PCA Services, Inc Durham, NC

Test condition : Animals: Forty four male B6C3F1 mice (6-7 weeks old) were acclimated for at least 7 days before exposure. All animals were examined on arrival for signs of ill health. Four sentinel animals had no evidence of infection. Animals were individually housed and were allowed free access to food and water (except during exposure, when they were with held). Four groups of 10 randomly allocated animals were used in the study.

Exposure conditions: Exposures were carried out in 1.5 m3 chambers constructed of stainless steel and glass. The breathing zone was ventilated at a rate of 12 air changes per hour. An additional chamber of 0.84 m3 capcacity was used for the air control group. The breathing zone of this chamber was ventilated at a rate of 6 air changes per hour. Compressed, filtered, conditioned and oil-free air was supplied through compressors fitted with automatic pressure control switches. Test atmospheres were exhausted from the exposure chambers with a Gast extract pump. The chambers were maintained under slight negative pressure to minimize leakage. Animal positions were rotated on a daily basis.

The test atmosphere was generated by bubbling dry, oxygen-free nitrogen through a liquid reservoir of 2-nitropropane immersed in a water bath maintained at 30 degrees C. Test material was added to the reservoir daily. The vapor mixture was ducted through stainless steel piping to a glass mising vessel and diluted with compressed air. The resulting mixture was piped to the top of the exposure chamber. Concentrations of test

material were maintained by regulating the flow of nitrogen and air into the mixing vessels using adjustable flowmeters.

Concentrations of test material in the atmospheres were analyzed by infrared spectroscopy (11.8 microns wavelength). Samples collected from the breathing zone were continuously pumped (5 l/min) through stainless steel sample lines to the gas cell of the analyzer. The analyzer was calibrated daily. The concentration was measured and relayed to a chart recorder.

Test conduct: Groups of animals were exposed to air (control), or 25 or 200 ppm test material 7 hours/day, for 5 days. Animals were observed for clinical signs after exposure. A positive control group was treated with 200 mg/kg ethylmethanesulphonate by gavage for 5 consecutive days. Positive control animals were not allowed access to food or water while the other animals were being exposed.

Mice were killed 5 weeks from the last expopsure day. The seminal ducts were exposed and the cauda epididymides were cut off. These were fixed with 2 ml of phosphate-buffere, 0.01% glutaraldehyde in 0.25 M sucrose. The cauda epididymides were finely minced and the sperm dispersed using a fine bore Pastuer pipette. The sperm were allowed to settle for 30 minutes in a centrifuge tube. After centrifugation at 500 rpm for 3 minutes, a few drops of the supernatant were spread onto a microscope slide. The slides were allowed to air dry overnight and were stained in 1% eosin in distilled water:ethanol (1:1) for 45 minutes. The slides were rinsed, air dried overnight on a hot plate, cleared in xyline for 5 minutes and mounted.

Sperm were scored under a microscope as being either normal or abnormal (with hook upturned or elongated, banana-shaped head, amorphous head, abnormal tail with sharp 180 degree angle or tight coiling, or miscellaneous). Sperm with multiple tails, double heads, twisted neck, filamentous midpiece, enlarged mid piece or plier type were scored under "miscellaneous". Sperm with separated tails and heads, clumps of sperm, sperm oriented such that the hook could not been seen or sperm partially masked by stain were not scored.

Statistical analyses: The data were transformed using the Freeman-Tukey transformation for proportions. A one-sided t test was used to analyze transformed values for numbers of abnormal sperm and each type of abnormal sperm.

Test substance : The test material had a stated purity of 94%. It was used as received from AMC Chemical Group Incorporated.

Reliability : (4) not assignable
The positive control did not cause an effect.

12.02.2004 (52)

5.9 SPECIFIC INVESTIGATIONS

Endpoint	:	other: hepatotoxicity
Study descr. in chapter	:	
Reference	:	
Type	:	
Species	:	mouse
Sex	:	male/female
Strain	:	Balb/c
Route of admin.	:	intraperitoneal
No. of animals	:	
Vehicle	:	other: DMSO in phosphate buffer solution

Exposure period	:	
Frequency of treatm.	:	single injection
Doses	:	4.5, 6.7, 9.0 mmol/kg
Control group	:	yes, concurrent vehicle
Observation period	:	96 hours
Result	:	
Method	:	
Year	:	1989
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Method : Nitroalkanes were dissolved in DMSO and then diluted with phosphate buffer to a pH~7.8. BALB/c mice were obtained from a commercial supplier and fed a commercial breeding diet. They were treated in dose groups of 3-5.

Mice were injected with the test cimpounds via the IP route in a volume of 0.2 mL. Mice were sacrificed at 24, 48, or 96 hours post-dosing, and plasma was assayed for measurements of sorbitol dehydrogenase (SDH), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). For histopathological investigation, livers were fixed, hydrated, and embedded. Sections from at least 3 lobes were cut and stained, and sections were evaluated blindly.

Result : A consistent finding was the absence of any effect in male mice 24 hours after dosing up to 9 mmol. Mean enzyme levels in plasma were elevated at 48 and 96 hours. Individual mice showed a striking variability in their succeptibility to the hepatotoxic effect of 2-NP, and there was a sex-dependent difference (females with larger increases in enzyme activity). The most severely affected livers showed an extensive hemorrhagic necrosis with apoptosis and disruption of the normal parenchyma. Mild proliferation of ductal-type cells in periportal areas was also noted. Less affected livers had single-cell necrosis, predominantly in a periportal location.

Reliability : (2) valid with restrictions
2 (meets generally accepted scientific standards, well-documented, and acceptable for assessment)

16.04.2005 (53)

5.10 EXPOSURE EXPERIENCE

Type of experience : Human - Epidemiology

Remark : The authors did not mention the excess of other lymphatic cancer in white males to be a significant finding (2 vs. 0.8 expected). However, they did mention it as being a significant finding in black males (2 vs. 0.2 expected).

It is interesting to note that cancer of the liver was not broken out as a category in this study, since this is the type of cancer that occurs in rats exposed to 2-nitropropane.

Result : White males: There were 94 deaths (versus 110.3 expected) in the 1066 white males employed between 1/1/1955 and 7/1/1977. The Standardized Mortility Ratio (SMR) of the employed white males was 85. The authors stated that the lowered mortality is a typical finding in an occupational cohort, since it does not include institutionalized subjects that contribute to general population mortality rates. Out of 13 categories [all cancers, seven types of cancers (digestive, respiratory, genitourinary, lymphatic and hematoietic, other lymphatic, and residual cancer), circulatory diseases, respiratory diseases, digestive diseases, external causes (motor vechile accidents, other accidents) and residual], the only categories that had

excess mortality in the employed group were external causes (22 vs. 18.7 expected), motor vechicle accidents (11 vs. 6.9 expected), and other lymphatic (2 vs. 0.8 expected).

Black males: There were 27 deaths (versus 40.6 expected) in the 268 black males employed between 1/1/1955 and 7/1/1977. The Standardized Mortility Ratio (SMR) of the employed black males was 67. The only significant finding ($p < 0.05$) was an increase in other lymphatic cancers in the employed males (2 vs. 0.2 expected). One of these deaths was attributed to mycosis fungoides and the other to "bleeding gastric ulcer-lymphosarcoma". The authors stated that is was unlikely that these two diseases are etiologically related.

Females: There were 8 deaths (versus 2.9 expected) in the 147 females employed between 1/1/1955 and 7/1/1977. The Standardized Mortility Ratio (SMR) of the females was 276. All causes of death examined were significantly higher than expected. Four cancer deaths occurred (versus 0.8 expected). One subject each reportedly died from buccal, respiratory, breast and residual cancers. Two subjects died from external causes and one each died from circulatory disease and "residual". Since the numbers of individuals dying from each cause were small, they did not appear to be related to employment.

Degree of Exposure (direct, indirect or none): There were no differences in the causes of death between individuals grouped according to degree of exposure to 2-nitropropane.

There were 7 deaths due to sarcomatous cancer (a relatively uncommon form). The tumors occurred in different sites and were therefore assigned to different categories. None of these deaths occurred among either directly or indirectly exposed workers.

Years of exposure: There were no clear trends between years of direct or indirect exposure to 2-nitropropane and the numbers of deaths. Among workers with more than 20 years latency (years between beginning of exposure and year of last follow up) there were 9 deaths (vs. 6.4 expected). If this same group was restricted those with more than 20 year's latency and 5 or more years of employment, there were 8 observed deaths and 5.1 expected. There was no suggestion of an excess of any particular cause of death in these individuals. Four of the eight deaths were due to cardiovascular disease and two to malignancy (unspecified primary site, lung cancer).

Person-years accumulated prior to 1955: There were no significant differences between expected and observed deaths in the 711 white males, 146 black males and 103 females who started working prior to 1/1/1955. There were no scarcomatous tumors in this group and the mortality of females was not elevated (in contrast to the post-1954 cohort).

Relationship to county of residence: Most of the employees lived in either Ouachita or Union Counties. The overall cancer rate in Ouachita county was similar to that of Louisiana and the whole United States, and the overall cancer rate in Union County was lower. Relative to the whole United States, residents of both counties had slightly lower age-adjusted rates of cancers of the GI tract. Relative to the United States and Louisiana, residents of both counties had slightly higher age-adjusted rates of skin cancer. Relative to the United States and Louisiana, residents of Ouachita County had slightly higher age-adjusted rates of leukemia and prostate cancer. None of the differences were sufficient enough to suggest a relationship between county of residence and occurrence of particular cancers.

Source : PCA Services, Inc Durham, NC

Test condition : Purpose: A retrospective mortality study was initated to determine if there were any unusual disease mortality patterns among Sterlington, Louisiana workers, either before or after the beinning of production of 2-nitropropane. The study included the 1,815 employees that had worked at the plant since 1946. Each death certificate was coded according to the eighth revision of the International Classification of Diseases. The purpose of the study was to determine if thesere were any unusual cancer or other disease mortality patterns among the workers.

Data: The following information was tabulated for each employee and stored in Computer Data File One: name, social security number, date of birth, military service, gender, ethnic group, date of pre-employment exam, medical history, socioeconom ic level, date of hire, date of entry in beginning department, date of termination, reason for termination, date of death (where applicable) and plant location. This information, plus address, personal habits (smoking, drinking), departments worked in, occupation in each department, dates of entry into each department, date of transfer and reason for change were entered and stored in Computer Data File Two.

Like information in Computer Data File Two was compared with Data File One. Error sheets were generated. Corrections were made by referral to the employee's file folder. All errors in this phase were eliminated.

Plant seniority (years of service) for each employee was verified using a data processing program. The individual's department seniority plus lay off time in Data File Two had to equal their plant seniority in Data File One within +/- 0.001 years. Plant seniority was calculated using June 30, 1977 or the data of termination (whichever was applicable), minus the data of hire. All errors in this phase were eliminated.

Using information from Data File Two, personnel roster runs were made for each 6 month period. The runs were developed by listing the beginning population for the period, adding the number of new hires and/or inter-company transferees in, and then subtracting the number of terminations and inter-company transferees out. The number of employees on the personnel roster for the period ending June 30, 1977 was identical to the actual population on that data. Upon completion of the rosters, Data File Two was considered to be the Master File.

Of the 180 deaths that occurred amoung the 1,815 employees, all of the death certificates (or the equivalent in the case of military deaths) were obtained. The causes of death were changed for 33 individuals in which the original code was considered incorrect. The living/dead status of past employees was determined for all but 11 individuals. Seven of these were terminated prior to 1955 and four after 1955.

Work activites of the employees were divided into 3 cohorts: direct exposure to 2-nitropropane (laboratory research, production, derivatives, and warehousing), indirect exposure (machine shop, electric shop, general maintenance, instrument shop, shipping, engineering, maintenance, technical service and process development) and no exposure (all other departments such as plant office and other processes). The number of employees in the respective groups was 372, 366 and 743.

Data were expressed as Standard Mortality Ratios (SMR). The SMR is the mathematical comparison between the observed deaths and expected deaths (derived from US mortality rates). It is calculated as observed deaths/expected deaths x 100.

A computer program estimated person-years of observation by color, sex, five year periods of age and time and applied US mortality rates in similar groupings.

Production of 2-nitropropane began in early 1955. Prior to 1955, there were 334 terminated employees. These employees had no possiblity of exposure to 2-nitropropane. The living/dead status was determined for 327 of these employees (98%).

Four individuals out of the 1,481 employees that were employed as of and/or after January 1, 1955 were not accounted for. These individuals worked in locations about 4 miles from the 2-nitropropane operations and had worked for < = 29 days.

Plant History: The plant manufactured materials other than 2-nitropropane. The period between January, 1946 and December, 1954 was a major growth period. The number of products and lines reached a maximum between 1955 through mid 1959. The number of employees remained fairly steady until around 1967, when it started to decrease due to discontinuation of certain product lines. The number of employees started to increase again after 1974 due to expansion of a material other than 2-nitropropane.

Prior to 1962, workplace 2-nitropropane levels were monitored via an informal subjective threshold evaluation. By 1962, workplace concentrations could be monitored. Periodically, concentrations in excess of the present TLV of 25 ppm were observed. The excursions (580 - 1640 ppm) occurred in the drumming area and coincided with the operators experiencing occassional headaches and symptoms of nausea. None of the symptoms required first aid or medical treatment by a doctor. Corrective measures taken to reduce exposure in drumming eliminated complaints of nausea and headache.

Prior to 1977, there was no formalized monitoring system to detect spills and/or leaks. For the first 6 months of 1977, monitored concentrations were 0.2 to 10 ppm (141/144 samples), 10 to 25 ppm (1/141 samples) and 25 to 100 ppm (2 spill area samples/144 total samples).

Conclusion : The authors concluded that there were no unusual cancer or other disease mortality pattern among the workers (either before of after the beginning of 2-mitropropane production in 1955). However, since the cohort was small and the period of latency was short for most of the subjects, the study did not prove that 2-nitropropane was not carcinogenic in humans. The authors recommended that the cohort should be followed and data should be analyzed periodically.

Reliability : (2) valid with restrictions
The relationship of exposure to cancers of the target organ of 2-nitropropane (the liver) were not analyzed separately.

17.02.2004 (54)

Type of experience : Human - Epidemiology

Remark : It was mentioned that a review of deaths caused by cancer revealed that no deaths resulted from cancer of liver (mlaignant neoplasm, or ICD code 155). This ICD classification includes hepatocellular carcinoma. Also, on o cases were reported indicating benign neoplasms (tumors) of the liver (ICD code 230.5).

Result : White males: There were 120 deaths (versus 152.3 expected) in the 1108 white males employed between 1/1/1955 and 1/1/1982. The Standardized Mortility Ratio (SMR) of the employed white males was 79 (which was typical for an occupational cohort). Out of 13 categories [all cancers, seven types of cancers (digestive, respiratory, genitourinary, lymphatic and

hematoi etic, other lymphatic, and residual cancer), circulatory diseases, respiratory diseases, digestive diseases, external causes (motor vechile accidents, other accidents) and residual], the only categories that had excess mortality in the employed group were external causes (29 vs. 23.4 expected) and motor vechicle accidents (13 vs. 8.2 expected). Neither of these differences reached statistical significance.

Black males: There were 33 deaths (versus 56.9 expected) in the 282 black males employed between 1/1 /1955 and 1/1/1982. The Standardized Mortility Ratio (SMR) of the employed black males was 58. The only significant finding ($p < 0.05$) was an increase in other lymphatic cancers in the employed males (2 vs. 0.2 expected). One of these deaths was attributed to mycosis fungoides and the other to "bleeding gastric ulcer-lymphosarcoma". These two deaths were present in the initial analysis performed in 1978.

Females: There were 8 deaths (versus 4.4 expected) in the 147 females employed between 1/1/1955 and 1/1/1982. There were no new deaths since the initial analysis. The Standardized Mortility Ratio (SMR) of the females was 183. All causes of death examined were significantly higher than expected. Four cancer deaths occurred (versus 0.8 expected). One subject each reportedly died from buccal, respiratory, breast and residual cancers. Two subjects died from external causes and one each died from circulatory disease and "residual". Since the numbers of individuals dying from each cause were small, they did not appear to be related to employment.

Degree of Exposure (direct, indirect or none): There were no differences in the causes of death between individuals grouped according to degree of exposure to 2-nitropropane.

There were 7 deaths due to sarcomatous cancer (a relatively uncommon form). The tumors occurred in different sites and were therefore assigned to different categories. None of these deaths occurred among either directly or indirectly exposed workers. This also was observed in the previous study. There were no new deaths due to sarcoma in this study.

Years of exposure: There were no clear trends between years of direct or indirect exposure to 2-nitropropane and the numbers of deaths. Unlike in the previous analysis, excess mortality did not occur among persons with 20 or more years of latency.

Person-years accumulated prior to 1955: This was not analyzed in this study.

Relationship to county of residence: This was not analyzed in this study.

Source : PCA Services, Inc Durham, NC

Test condition : The protocol and cohort selection described in the previous ecord were followed in this update, with the distribution of the number of employees in the 3 cohorts as of January 1, 1955 (when production of 2-nitropropane began) through December 31, 1981 as 400 (direct), 406 (indirect) and 773 (no exposure), for a total of 1,579. The total of employees that had worked at the plant since 1946 was 1,915.

Data compilation and verification were the same as in the prvious report, with the exception that no information on personal habits of drinking and smoking was tabulated.

Of the 223 deaths that occurred among the 1,915 employees, all of the death certificates (Or the equivalent in the case of military deaths) were obtained. The codes for underlying cause of death were reviewed and

corrected in 21 instances.

The living/dead stautus of past employees was determined for all abut 9 individuals. Seven of these were terminated prior to 1955 and two after 1955. Prior to 1955, there were 336 terminated employees. These employees had no possibility of any exposure to 2-nitropropane. The living/dead status was determined for 329 of these employees (98%).

The living/dead status of the 1,579 employees that were employed as of and/or after January 1, 1955 was 1,415 alive and 162 dead. Two were not accounted for. Therefore, the accountability rate was 99.8%.

As in the previous study, the purpose of the study was to classify the cause of death according to the Eighth Revision of the International Classification of Diseases (ICD) and determined if there were any unusual cancers or other disease mortality patterns among the workers.

Conclusion : The authors concluded that there were no unusual cancer or other disease mortality pattern among the workers. However, since only 10% of the study population was deceased, further followup was recommended.

Reliability : (2) valid with restrictions
The conclusions of this study are relevant for the cohort examined but do not prove that exposure to 2-nitropropane does not cause cancer in humans.

17.02.2004 (55)

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT